=> d his

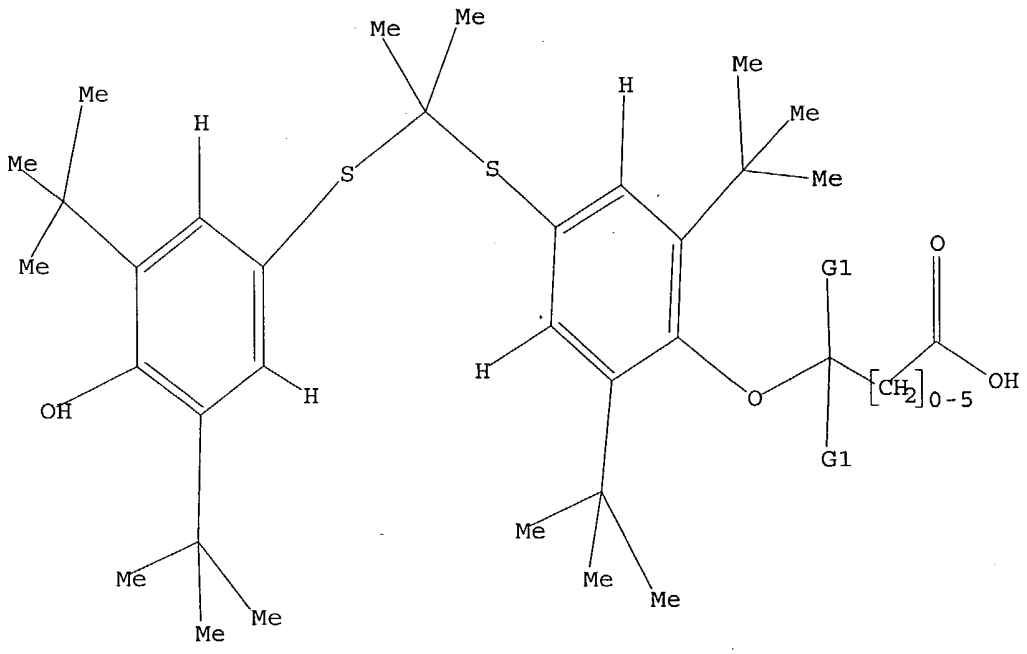
(FILE 'HOME' ENTERED AT 15:07:30 ON 20 SEP 2004)

FILE 'REGISTRY' ENTERED AT 15:07:41 ON 20 SEP 2004
L1 STRUCTURE UPLOADED
L2 0 S L1 SSS
L3 0 S L1 SSS FULL
L4 STRUCTURE UPLOADED
L5 0 S L4 SSS
L6 0 S L4 SSS FULL
L7 STRUCTURE UPLOADED
L8 0 S L7 SSS
L9 0 S L7 SSS FULL
L10 STRUCTURE UPLOADED
L11 0 S L10 SSS
L12 0 S L10 SSS FULL
L13 STRUCTURE UPLOADED
L14 0 S L13 SSS
L15 0 S L13 SSS FULL

FILE 'REGISTRY' ENTERED AT 15:23:31 ON 20 SEP 2004
L16 STRUCTURE UPLOADED
L17 1 S L16 SSS
L18 12 S L16 SSS FULL
L19 STRUCTURE UPLOADED
L20 3 S L19 SSS
L21 34 S L19 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:28:12 ON 20 SEP 2004
L22 6 S L18
L23 24 S L21
L24 24 S L22 OR L23

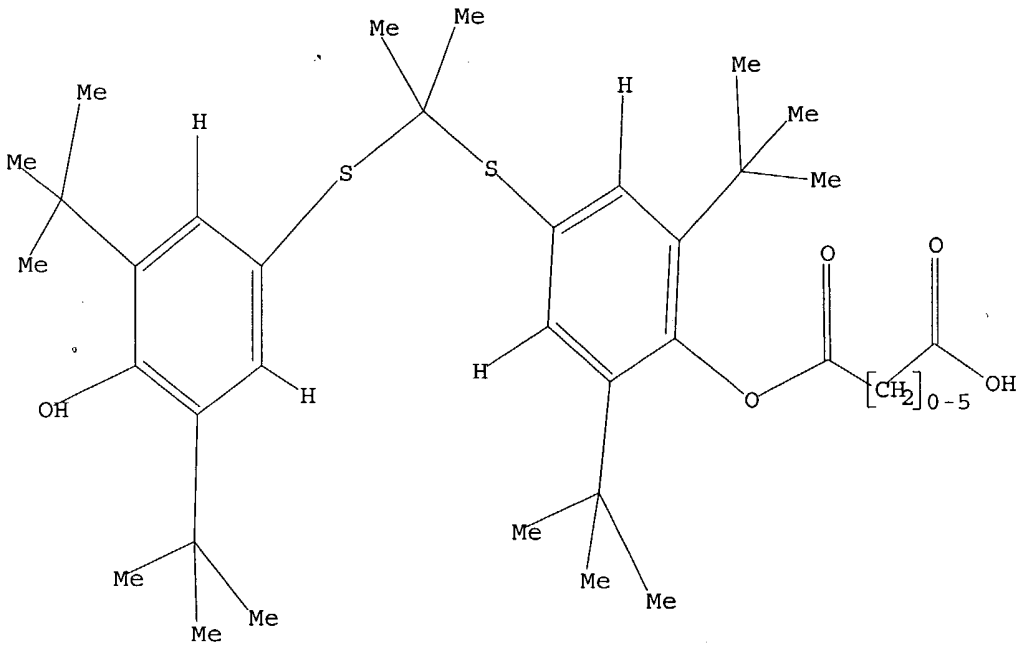
=> d l16
L16 HAS NO ANSWERS
L16 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> d l19
L19 HAS NO ANSWERS
L19 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

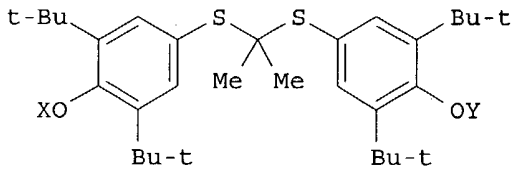
=> d l24 bib abs hitstr 1-24

L24 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:610066 CAPLUS
DN 141:156929
TI Process of preparing esters and ethers of probucol and derivatives thereof
IN Weingarten, M. David; Sikorski, James A.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004062622	A2	20040729	WO 2004-US805	20040113

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRAI US 2003-439665P P 20030113
GI



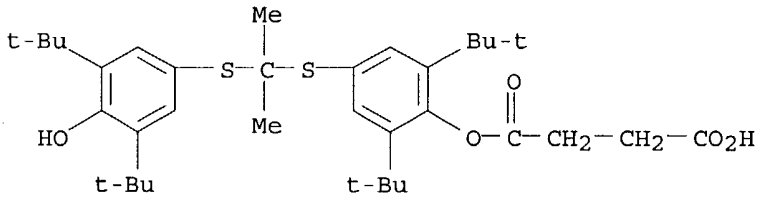
I

AB Probucol or a probucol derivative can be efficiently converted to a monoester or monoether of probucol (I) [wherein R1-R4 = H, (un)substituted alkyl; R5, R6 = each (un)substituted alkyl, alkenyl, or aryl; or R5 and R6 can come together to form a carbocyclic ring; X, Y = H, optionally substituted (un)saturated acyl having from 1 to 18 carbon atoms each optionally containing a polar or charged functionality] by reacting the free hydroxyl-containing probucol or a derivative thereof (by which is meant a probucol compound with at least one substituent that is different from that on the parent probucol mol. but which maintains the two free hydroxyl groups), i.e., I (X = Y = H; R1-R6 = same as above), with a Grignard reagent or a lithium reagent that produces a magnesium bromide or lithium salt of probucol or the probucol derivative The probucol compound anion is then reacted with an ester or ether forming compound Thus, in a dry 25 mL 3-neck round bottom flask fitted with a reflux condenser, nitrogen inlet, thermocouple and stir bar was charged probucol (0.25 g, 0.48 mmol) followed by 2.5 mL anhydrous toluene and then isopropylmagnesium chloride (0.51 mL, 2.0 M in THF) in 1 portion. The reaction was brought to room temperature and then succinic anhydride (0.25 g, 2.5 mmol) was added in 1 portion. After aging for 45 min, the reaction was slowly quenched with 1 N HCl and diluted with EtOAc. The biphasic reaction was then cooled to room temperature and the phases were separated to give an organic layer containing 60% probucol monosuccinate, 13% probucol disuccinate, and 27% probucol according to HPLC anal.

IT **216167-82-7P**, Probucol monosuccinate **216167-92-9P** **216167-95-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of esters and ethers of probucol and its derivs. by treatment of probucol and its derivs. with Grignard reagent or organolithium reagent and then ester or ether forming compound)

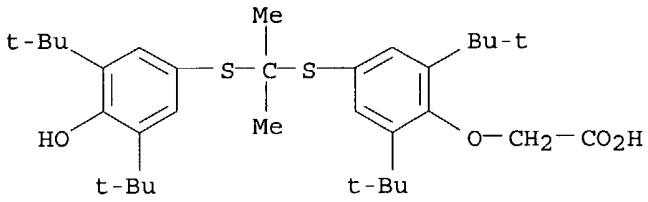
RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

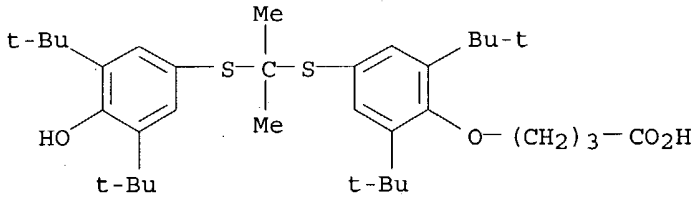


RN 216167-92-9 CAPLUS

CN Acetic acid, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 216167-95-2 CAPLUS
CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



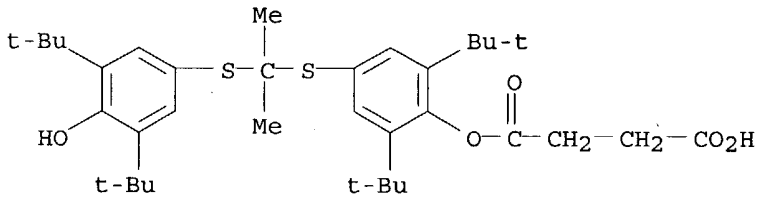
L24 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:181454 CAPLUS
DN 140:332096
TI Selective inhibition of endothelial and monocyte redox-sensitive genes by AGI-1067: A novel antioxidant and antiinflammatory agent
AU Kunsch, Charles; Luchoomun, Jayraz; Grey, Janice Y.; Olliff, Lynda K.; Saint, Leigh B.; Arrendale, Richard F.; Wasserman, Martin A.; Saxena, Uday; Medford, Russell M.
CS Department of Discovery Research, AtheroGenics, Inc., Alpharetta, GA, USA
SO Journal of Pharmacology and Experimental Therapeutics (2004), 308(3), 820-829
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Atherosclerosis is a disease of oxidative stress and inflammation. AGI-1067 [butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-,hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester] is a metabolically stable derivative of, yet pharmacol. distinct from, the antioxidant drug probucol. It is a member of a novel class of orally active, antioxidant, anti-inflammatory compds. termed vascular protectants and exhibits antiatherosclerotic properties in multiple animal models and in humans. To elucidate its antiatherosclerotic mechanisms, we have evaluated several cellular and mol. properties of AGI-1067 in vitro. AGI-1067 exhibited potent lipid peroxide antioxidant activity comparable with probucol yet demonstrated significantly enhanced cellular uptake over that observed with probucol. AGI-1067, but not probucol, inhibited basal levels of reactive oxygen species (ROS) in cultured primary human endothelial cells and both basal and hydrogen peroxide-induced levels of ROS in the promonocytic cell line, U937. Furthermore, AGI-1067 inhibited the inducible expression of the redox-sensitive genes, vascular cell adhesion mol.-1 (VCAM-1) and monocyte chemoattractant protein-1, in endothelial cells as well as tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, and IL-6 production in peripheral blood mononuclear cells, whereas probucol had no effect. CDNA array hybridization expts. demonstrated that AGI-1067 selectively inhibited the expression of only a subset of TNF-α-responsive and nuclear factor-κB (NF-κB)-inducible genes in endothelial cells. The inhibitory effect of AGI-1067 on inducible VCAM-1 gene expression occurred at the

transcriptional level, yet AGI-1067 had no effect on the activation of the redox-sensitive transcription factor NF-κB. These studies suggest that the anti-inflammatory and antiatherosclerotic properties of AGI-1067 may be due to selective inhibition of redox-sensitive endothelial and monocyte inflammatory gene expression. These studies provide a mol. basis for understanding the mechanism of action of this new class of therapeutic antiatherosclerotic compds.

IT **216167-82-7**, AGI-1067
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective inhibition of endothelial and monocyte redox-sensitive genes by an antiinflammatory and antioxidant agent, AGI-1067)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:60447 CAPLUS
DN 140:105287
TI Preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders
IN Meng, Charles Q.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004007423	A1	20040122	WO 2003-US21781	20030714
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004082807	A1	20040429	US 2003-619268	20030714
PRAI	US 2002-395573P	P	20020712		

AB Organic amine salts of probucol esters and ethers, especially meglumine salts of compds. such as 4-[4-[[1-[[3,5-bis-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]butanoic acid (I), are for the treatment of inflammatory disorders, e.g., arthritis, asthma, multiple sclerosis,

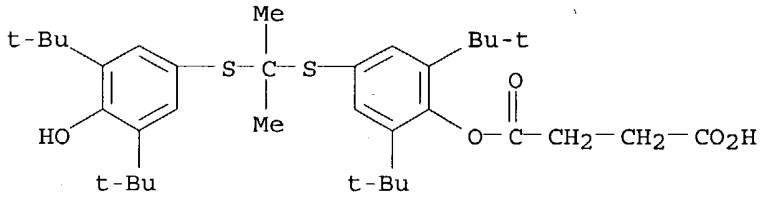
psoriasis, etc. Thus, a probucol ester salt was prepared by the treatment of I with meglumine in in THF solution Th effectiveness of the compound in the treatment of inflammatory disorders was demonstrated.

IT **646518-18-5P 646518-19-6P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders)

RN 646518-18-5 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl butanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

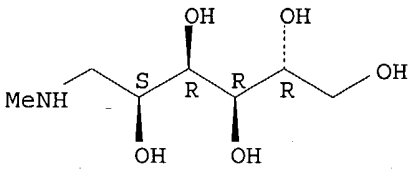
CRN 216167-82-7
CMF C35 H52 O5 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

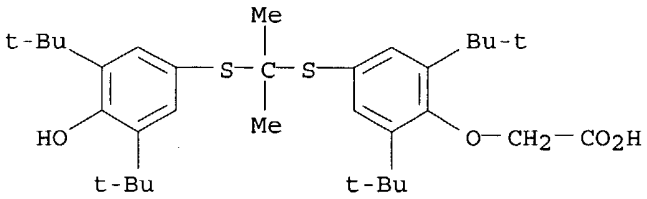
Absolute stereochemistry.



RN 646518-19-6 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]acetate (salt) (9CI) (CA INDEX NAME)

CM 1

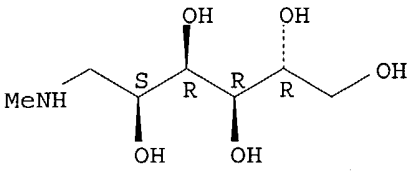
CRN 216167-92-9
CMF C33 H50 O4 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

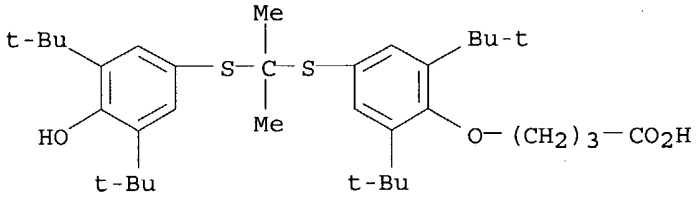
Absolute stereochemistry.



IT **646518-20-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders)
RN 646518-20-9 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]butanoate (salt) (9CI) (CA INDEX NAME)

CM 1

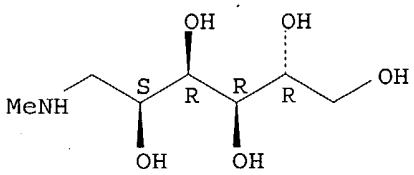
CRN 216167-95-2
CMF C35 H54 O4 S2



CM 2

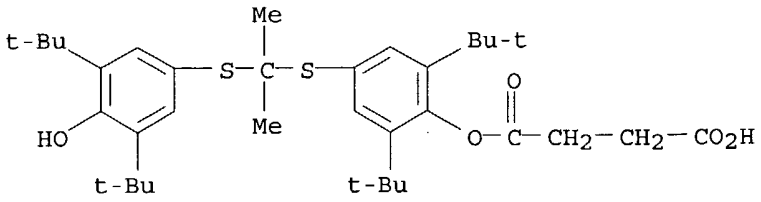
CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

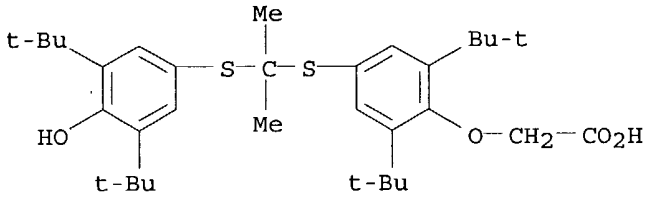


IT **216167-82-7 216167-92-9 216167-95-2**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-

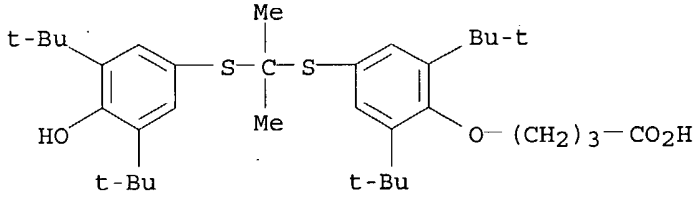
hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 216167-92-9 CAPLUS
CN Acetic acid, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



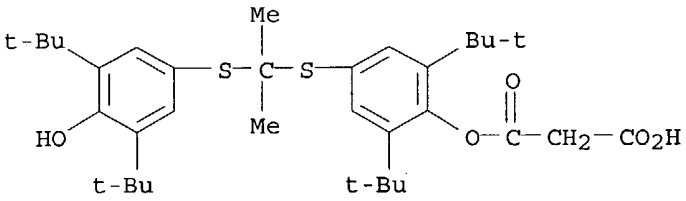
RN 216167-95-2 CAPLUS
CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



IT **646518-21-0P 646518-22-1P 646518-23-2P**
646518-25-4P 646518-27-6P 646518-28-7P
646518-30-1P 646518-32-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders)
RN 646518-21-0 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl propanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

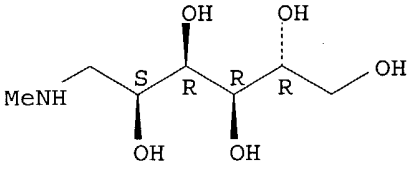
CRN 524005-22-9
CMF C34 H50 O5 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

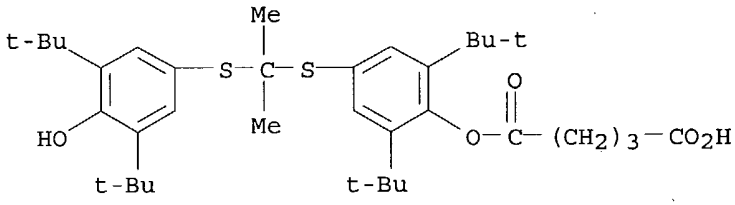
Absolute stereochemistry.



RN 646518-22-1 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl pentanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

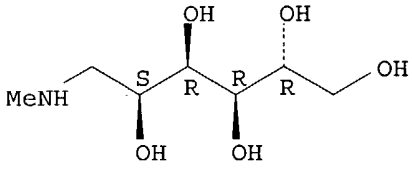
CRN 216167-94-1
CMF C36 H54 O5 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

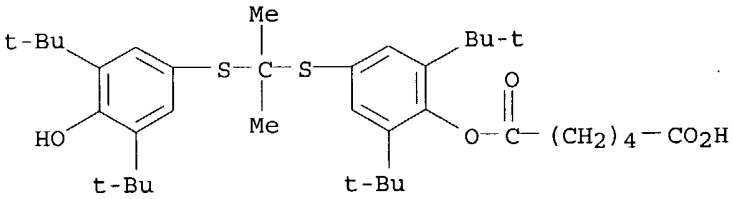


RN 646518-23-2 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl

hexanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

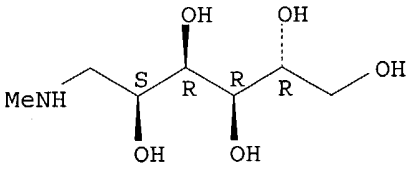
CRN 219773-26-9
CMF C37 H56 O5 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

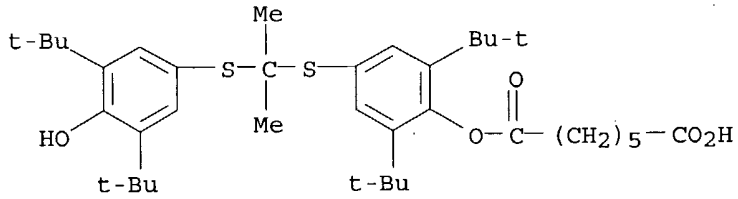
Absolute stereochemistry.



RN 646518-25-4 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl heptanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

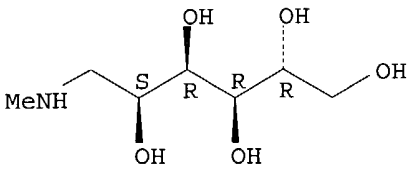
CRN 646518-24-3
CMF C38 H58 O5 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

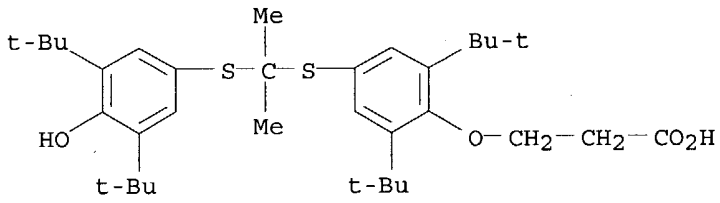
Absolute stereochemistry.



RN 646518-27-6 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 3-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]propanoate (salt) (9CI) (CA INDEX NAME)

CM 1

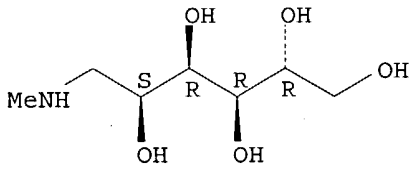
CRN 646518-26-5
CMF C34 H52 O4 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

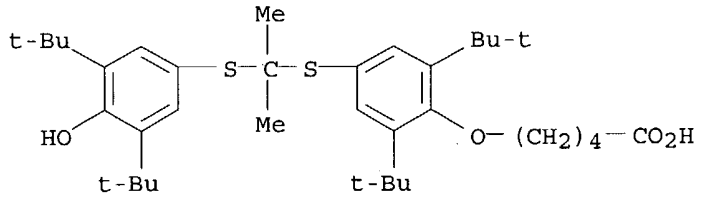
Absolute stereochemistry.



RN 646518-28-7 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 5-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]pentanoate (salt) (9CI) (CA INDEX NAME)

CM 1

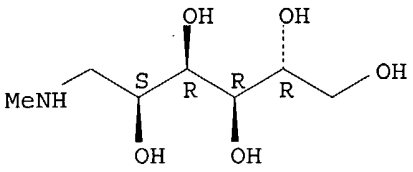
CRN 216168-44-4
CMF C36 H56 O4 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

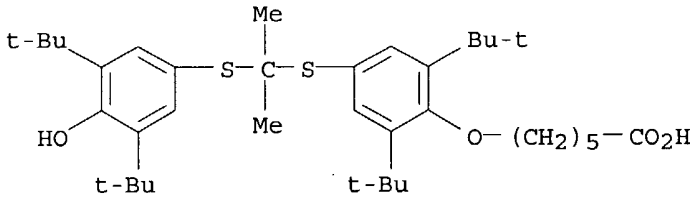
Absolute stereochemistry.



RN 646518-30-1 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 6-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]hexanoate (salt) (9CI) (CA INDEX NAME)

CM 1

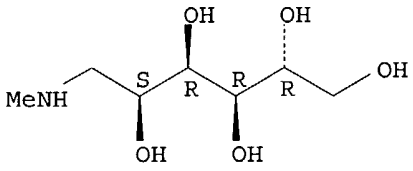
CRN 646518-29-8
CMF C37 H58 O4 S2



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

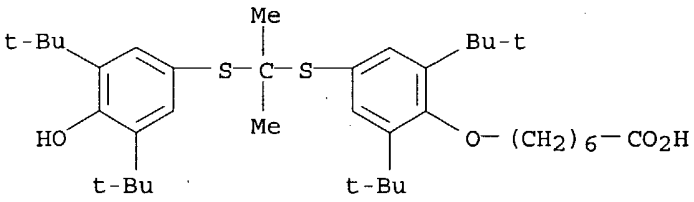
Absolute stereochemistry.



RN 646518-32-3 CAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, 7-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]heptanoate (salt) (9CI) (CA INDEX NAME)

CM 1

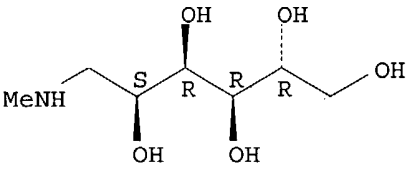
CRN 646518-31-2
CMF C38 H60 O4 S2



CM 2

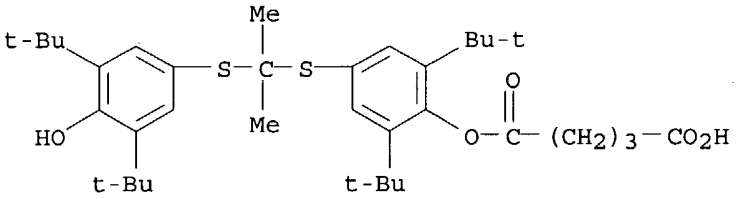
CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

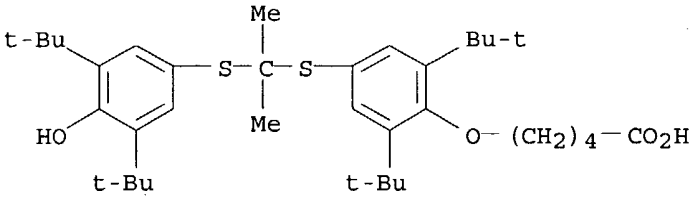


IT **216167-94-1 216168-44-4 219773-26-9**
524005-22-9 646518-24-3 646518-26-5
646518-29-8 646518-31-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of meglumine salts of poorly soluble probucol esters and ethers for treatment of inflammatory disorders)

RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

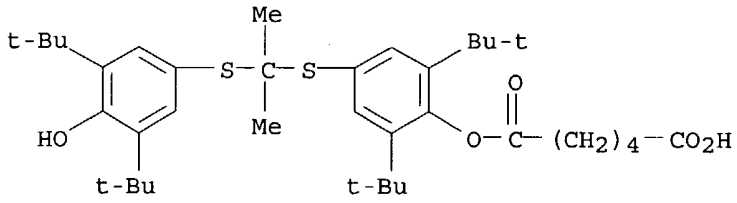


RN 216168-44-4 CAPLUS
CN Pentanoic acid, 5-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)

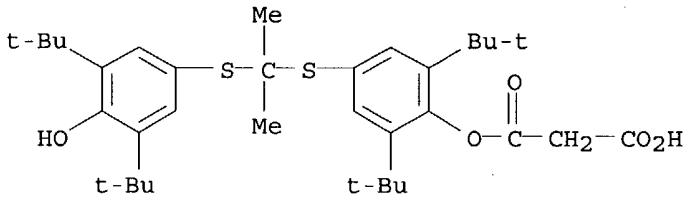


RN 219773-26-9 CAPLUS
CN Hexanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl]

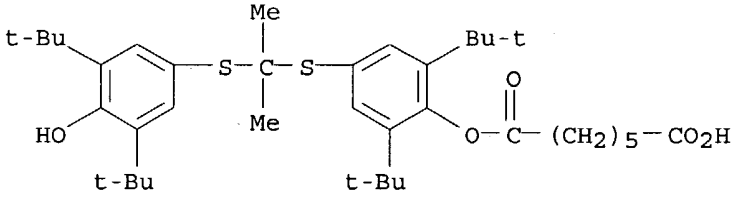
ester (9CI) (CA INDEX NAME)



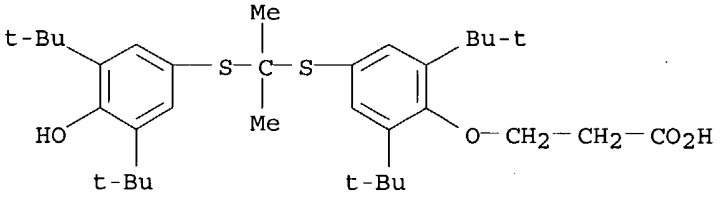
RN 524005-22-9 CAPLUS
CN Propanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



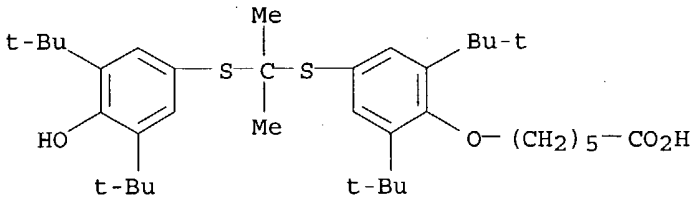
RN 646518-24-3 CAPLUS
CN Heptanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



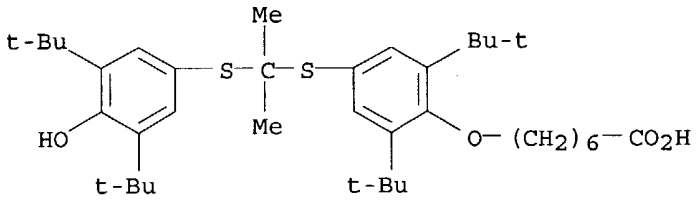
RN 646518-26-5 CAPLUS
CN Propanoic acid, 3-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 646518-29-8 CAPLUS
CN Hexanoic acid, 6-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 646518-31-2 CAPLUS
CN Heptanoic acid, 7-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

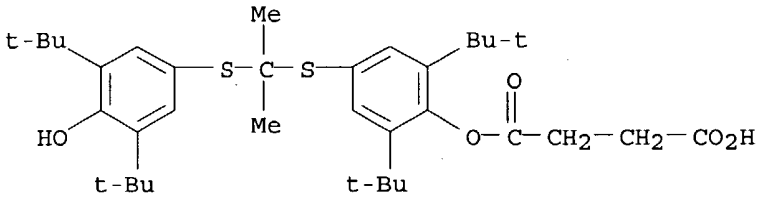
L24 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:904519 CAPLUS
DN 140:331520
TI Pharmacologic prevention of both restenosis and atherosclerosis progression: AGI-1067, probucol, statins, folic acid, and other therapies
AU Tardif, Jean-Claude; Gregoire, Jean; Lavoie, Marc-Andre; L'Allier, Philippe L.
CS Department of Medicine, Montreal Heart Institute, Montreal, Can.
SO Current Opinion in Lipidology (2003), 14(6), 615-620
CODEN: COPLEU; ISSN: 0957-9672
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
AB A review. In this article, the authors intend to provide an update on clin. trials of pharmacol. prevention of restenosis after percutaneous coronary interventions, placed in the perspective of the use of orally administered therapy for the prevention of atherosclerosis progression and clin. events. AGI-1067, the mono-succinic acid ester of probucol, is a phenolic antioxidant member of a novel class of agents termed v-protectants. It has strong antioxidant properties equipotent to those of probucol and antiinflammatory properties. It inhibits gene expression of VCAM-1 and MCP-1 and was effective at preventing atherosclerosis in all tested animal models including the non-human primate. In the Canadian Antioxidant Restenosis Trial (CART) 1, AGI-1067 and probucol improved lumen dimensions at the site of percutaneous coronary intervention. AGI-1067 also improved luminal dimensions of non-intervened coronary reference segments in the Canadian Antioxidant Restenosis Trial, which suggests a direct antiatherosclerosis effect. Probucol reduced post-percutaneous coronary intervention restenosis and progression of carotid atherosclerosis in other clin. trials. Although statins reduce atherosclerotic events, they do not appear to have a significant effect on restenosis. The failure of folate therapy to protect against restenosis in the Folate After Coronary Intervention Trial (FACIT) occurred despite significant redns. in Hcy levels. Prevention of both post-percutaneous coronary intervention restenosis and atherosclerosis progression with a pharmacol. agent such as AGI-1067 may be an attractive treatment paradigm. Two important trials that test the antioxidant/antiinflammatory hypothesis

are ongoing with AGI-1067: the Canadian Atherosclerosis and Restenosis Trial 2, which assesses its value for the reduction of both atherosclerosis progression and post-percutaneous coronary interventions restenosis, and the Aggressive Reduction of Inflammation Stops Events (ARISE) trial which is evaluating its effects on cardiovascular events.

IT **216167-82-7**, AGI-1067
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention of both restenosis and atherosclerosis progression)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:845461 CAPLUS

DN 140:192654

TI Experimental and clinical studies show that the probucol derivative AGI-1067 prevents vascular growth

AU Doggrell, Sheila A.

CS Doggrell Biomedical Communications, Auckland, Lynfield, N. Z.

SO Expert Opinion on Investigational Drugs (2003), 12(11), 1855-1859
CODEN: EOIDER; ISSN: 1354-3784

PB Ashley Publications Ltd.

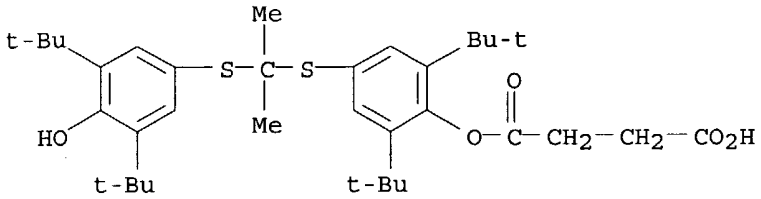
DT Journal

LA English

AB AGI-1067 is a derivative of probucol that is a promising new development for the treatment of restenosis and possibly atherosclerosis. In monkeys fed a high-fat diet for 1 yr, AGI-1067 prevented the development of atherosclerosis. In these monkeys, AGI-1067 lowered plasma levels of low-d. lipoprotein (LDL)-cholesterol and, in contrast to probucol, was capable of increasing high-d. lipoprotein (HDL)-cholesterol levels. Although AGI1067 did not have marked lipid-lowering effects in two transgenic mouse models (the LDL-receptor-deficient and apolipoprotein-E-deficient models) fed a high-fat chow, it decreased the atherosclerotic lesion area in the aorta. In a mouse model of acute inflammation, the mRNA for the pro-inflammatory vascular cell adhesion mol.-1 and monocyte chemoattractant protein-1 was upregulated and this was inhibited by AGI-1067. AGI-1067 inhibited the TNF-α induction of redox-sensitive inflammatory proteins, vascular cell adhesion mol.-1, monocyte chemoattractant protein-1 and E-selectin, in cell culture. In addition, AGI-1067 is an antioxidant. In the Canadian Antioxidant Restenosis Trial (CART-1) of AGI-1067 in percutaneous coronary interventions, AGI-1067 had no effect on LDL-cholesterol but lowered HDL-cholesterol. At 6 mo follow up, the lumen area of the percutaneous coronary interventions segments was greater in patients treated with AGI1067 than in untreated patients. Restenosis rates were 37.5% in the placebo group and 26% in the AGI-1067 group. The lumen area of reference segments was reduced in the placebo group but increased with the higher doses of AGI1067. Unlike probucol, AGI-1067 did not alter QTc interval.

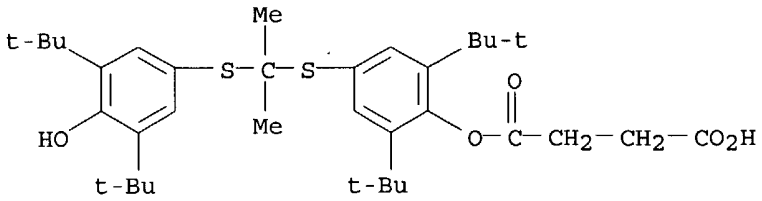
IT **216167-82-7**, AGI-1067
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(exptl. and clin. studies show that the probucol derivative AGI-1067 prevents vascular growth)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:803403 CAPLUS
DN 139:332164
TI Vascular protectants for the treatment of atherosclerosis
AU Tardif, Jean-Claude; Gregoire, Jean; Lavoie, Marc-Andre; L'Allier, Philippe L.
CS Clin. Res., Montreal Heart Inst., Montreal, QC, H1T 1C8, Can.
SO Expert Review of Cardiovascular Therapy (2003), 1(3), 385-392
CODEN: ERCTAS; ISSN: 1477-9072
PB Future Drugs Ltd.
DT Journal; General Review
LA English
AB A review. AGI-1067, the monosuccinic acid ester of probucol, is a phenolic antioxidant member of a novel class of agents termed vascular protectants. It has strong antioxidant properties, equipotent to those of probucol, and anti-inflammatory properties. It inhibits gene expression of vascular cell adhesion mol.-1 and monocyte chemotactic protein-1 and has been effective at preventing atherosclerosis in all tested animal models. It also improved luminal dimensions of reference segments in the percutaneous coronary intervention (PCI) vessels in the CART-1 clin. trial, which suggests a direct anti-atherosclerosis effect. Two important trials that test the antioxidant/anti-inflammatory hypothesis are ongoing with AGI-1067: the Canadian Atherosclerosis and Restenosis Trial, which assesses its value for the reduction of both atherosclerosis progression in non-PCI vessels and post-PCI restenosis, and the Aggressive Reduction of Inflammation Stops Events trial, which is evaluating the effects of AGI-1067 on hard cardiovascular outcomes.
IT **216167-82-7**, AGI-1067
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of vascular protectant AGI-1067 for treatment of atherosclerosis)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

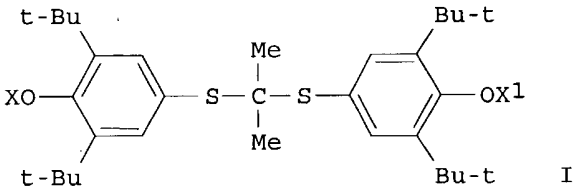
L24 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:777753 CAPLUS
DN 139:276712
TI Preparation of probucol derivatives for treatment of hyperlipidemia, inflammatory disorders, etc.
IN Del Soldato, Piero; Santus, Giancarlo; Ongini, Ennio
PA Nicox S.A., Fr.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003080568	A2	20031002	WO 2003-EP2850	20030319

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

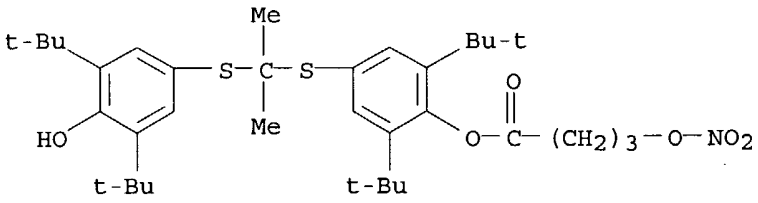
PRAI IT 2002-MI597 A 20020322
OS MARPAT 139:276712
GI



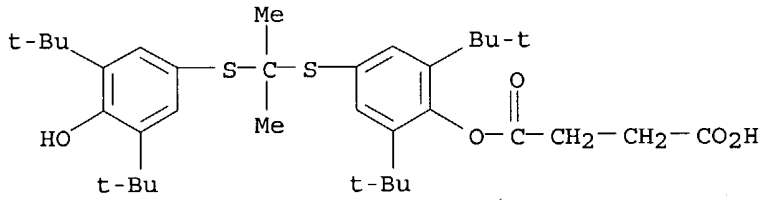
I

AB The title compds. I [X, X1 = H, (T)nYNO2; X and X1 cannot be both H; n = 0 or 1; when n = 1, T = CO; Y = bivalent radical (further details on this bivalent radical are given)], useful in the treatment of hyperlipidemia, inflammatory disorders (no data), etc., are prepared
IT **607393-84-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of probucol derivs. for treatment of hyperlipidemia and inflammatory disorders)
RN 607393-84-0 CAPLUS

CN Butanoic acid, 4-(nitrooxy)-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:704642 CAPLUS
DN 139:285453
TI AGI-1067: Treatment of atherosclerosis VCAM-1 and MCP-1 expression inhibitor antioxidant
AU Sorbera, L. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2003), 28(5), 421-424
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. AGI-1067 is a monosuccinate ester of probucol that exhibited marked lipid-lowering and antioxidant activity. AGI-1067 potently inhibited VCAM-1 and MCP-1 expression and smooth muscle cell proliferation and was effective in animal models of atherosclerosis and hyperlipidemia. The agent has shown efficacy in the prevention of atherosclerosis in patients with coronary artery disease and in preventing restenosis in patients undergoing percutaneous coronary interventions. AG-1067 is currently undergoing phase III trials with an indication for secondary prevention of atherosclerotic cardiovascular disease.
IT **216167-82-7**, AGI-1067
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VCAM-1 and MCP-1 expression inhibitor and antioxidant AGI-1067 for treatment of atherosclerosis)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:420448 CAPLUS
DN 139:224371
TI AGI-1067: A multifunctional phenolic antioxidant, lipid modulator, anti-inflammatory and antiatherosclerotic agent

AU Sundell, Cynthia L.; Somers, Patricia K.; Meng, Charles Q.; Hoong, Lee K.; Suen, Ki-Ling; Hill, Russell R.; Landers, Laura K.; Chapman, Angela; Butteiger, Dustie; Jones, Moira; Edwards, David; Daugherty, Alan; Wasserman, Martin A.; Alexander, R. Wayne; Medford, Russell M.; Saxena, Uday

CS AtheroGenics, Inc., Alpharetta, GA, USA

SO Journal of Pharmacology and Experimental Therapeutics (2003), 305(3), 1116-1123
CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

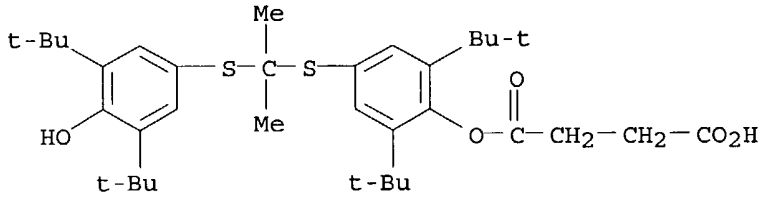
LA English

AB To explore the therapeutic efficacy and potential mechanisms of action of a new class of antiatherosclerotic drugs, AGI-1067 [mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1- methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester] (butanedioic acid) was tested in several animal models of atherosclerosis. AGI-1067, a novel phenolic antioxidant, was well tolerated in a 1-yr study in hypercholesterolemic cynomolgus monkeys. It lowered low-d. lipoprotein cholesterol (LDLc) by 41 and 90% at oral doses of 50 and 150 mg/kg, resp. and increased high-d. lipoprotein cholesterol (HDLc) by 107% at the higher dose. In contrast, another phenolic antioxidant, probucol, had a modest LDLc-lowering effect (15% at 250 mg/kg) while decreasing HDLc (37% at 150 mg/kg). Histopathol. of the aortas and coronary arteries revealed no atherosclerosis in the AGI-1067 (150 mg/kg) group and minimal-to-moderate atherosclerosis in the vehicle and probucol (150 mg/kg) groups. AGI-1067 also inhibited atherosclerosis in LDL receptor-deficient (LDLr -/-) mice and apolipoprotein E-deficient (ApoE -/-) mice even in the absence of a lipid-lowering effect. In LDLr -/- mice, AGI-1067 reduced aortic atherosclerosis by 49%. In ApoE -/- mice, AGI-1067 reduced atherosclerosis by 25, 41, and 49% in the arch, thoracic, and abdominal regions of the aorta. AGI-1067 also reduced vascular cell adhesion mol.-1 (VCAM-1) and monocyte chemoattractant protein-1 (MCP-1) mRNA levels in lungs of lipopolysaccharide-stimulated mice. At the cellular level, AGI-1067 inhibited tumor necrosis factor-α-inducible expression of VCAM-1, MCP-1, and E-selectin in human aortic endothelial cells (IC50 values = 6, 10, and 25 μM, resp.). These data show that AGI-1067 can inhibit atherosclerosis not only via its lipid-lowering effects but also by having direct anti-inflammatory effects on the vessel wall and suggest that it may be a novel therapeutic agent for coronary artery disease.

IT **216167-82-7**, AGI-1067
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AGI-1067 as a multifunctional phenolic antioxidant, lipid modulator, anti-inflammatory and antiatherosclerotic agent)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



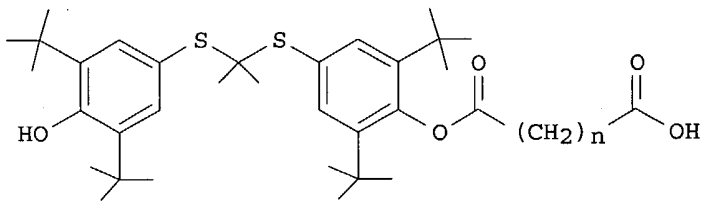
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 24 CAPLUS

AN 2003:376540 CAPLUS
DN 138:362685
TI Methods of reversing and preventing cardiovascular pathologies
IN Glass, Mitchell; Tardif, Jean-Claude
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003039352	A2	20030515	WO 2002-US37274	20021112
	WO 2003039352	A3	20031023		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003181520	A1	20030925	US 2002-293399	20021112
	EP 1451138	A2	20040901	EP 2002-789782	20021112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI	US 2001-347778P	P	20011109		
	WO 2002-US37274	W	20021112		

OS MARPAT 138:362685
GI

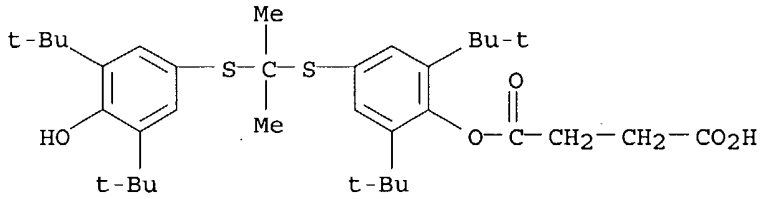


I

AB The present invention is a method to increase the lumen diameter of a coronary blood vessel, that includes administering a lumen increasing amount of a compound of the formula I wherein x is defined as an integer between 1 and 4; or a pharmaceutically acceptable salt, ester or prodrug thereof.

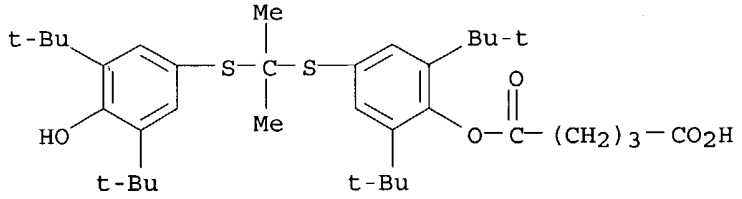
IT **216167-82-7P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of reversing and preventing cardiovascular pathol. associated with decrease in lumen diameter of coronary blood vessel in combination with other agents without prolongation of the heart QTc interval)

RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

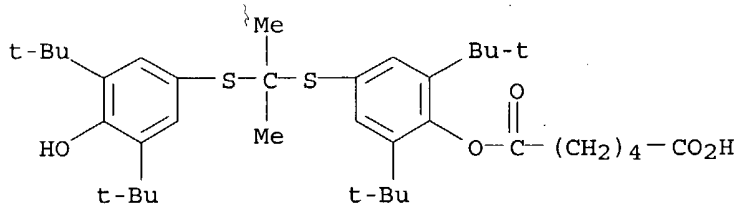


IT **216167-94-1 219773-26-9 524005-22-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of reversing and preventing cardiovascular pathol. associated with decrease in lumen diameter of coronary blood vessel in combination with other agents without prolongation of the heart QTc interval)

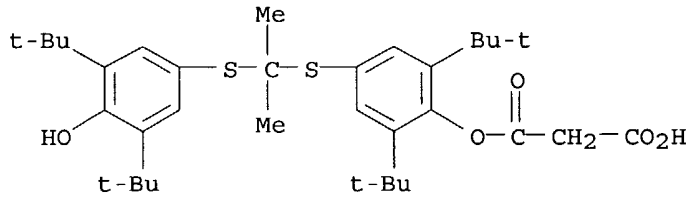
RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 219773-26-9 CAPLUS
CN Hexanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 524005-22-9 CAPLUS
CN Propanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

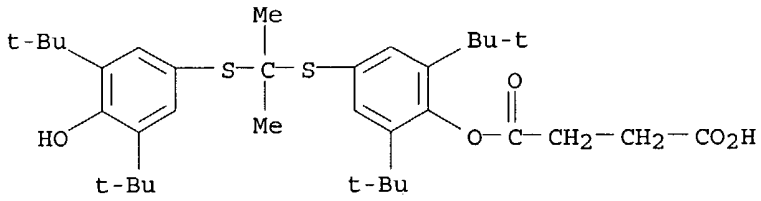


L24 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

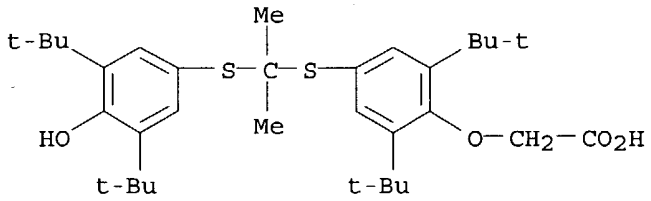
AN 2003:376511 CAPLUS
DN 138:362670
TI Probucol-related compounds and methods for treating transplant rejection
IN Glass, Mitchell; Edwards, David B.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003039231	A2	20030515	WO 2002-US34187	20021025
	WO 2003039231	A3	20031016		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003153536	A1	20030814	US 2002-281027	20021025
	EP 1446113	A2	20040818	EP 2002-802807	20021025
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI	US 2001-339535P	P	20011025		
	WO 2002-US34187	W	20021025		

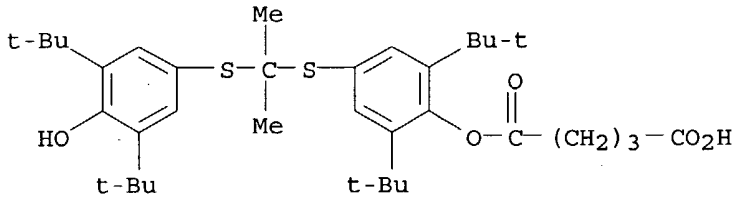
OS MARPAT 138:362670
AB The invention discloses the use of probucol-related compds. (Markush included), and pharmaceutically acceptable salts thereof, alone or in combination, for the treatment of transplant rejection.
IT **216167-82-7 216167-92-9 216167-94-1**
216167-95-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(probucol-related compds. for treating transplant rejection)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



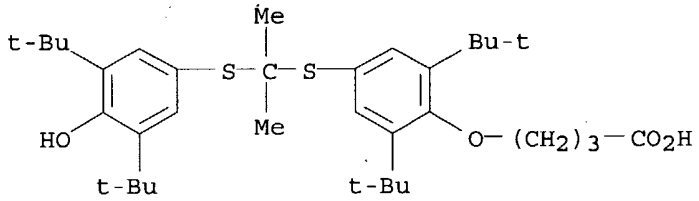
RN 216167-92-9 CAPLUS
CN Acetic acid, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 216167-95-2 CAPLUS
CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



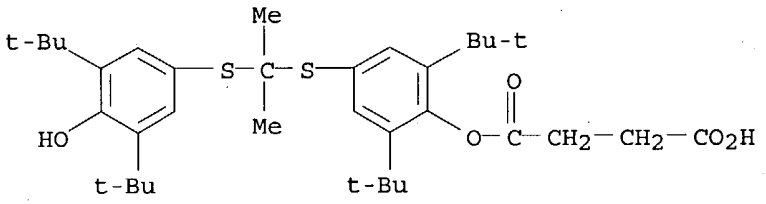
L24 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:201721 CAPLUS
DN 139:269969
TI Clinical results with AGI-1067: a novel antioxidant vascular protectant
AU Tardif, Jean-Claude
CS Department of Medicine, Montreal Heart Institute, Montreal, QC, H1T 1C8, Can.
SO American Journal of Cardiology (2003), 91(3A), 41A-49A
CODEN: AJCDAG; ISSN: 0002-9149
PB Excerpta Medica, Inc.
DT Journal; General Review
LA English
AB A review. A large body of evidence points to oxidative stress as an important trigger in the complex chain of events leading to atherosclerosis. Reactive O species have also been implicated in the pathophysiol. of restenosis after percutaneous coronary interventions (PCI). The powerful antioxidant probucol has been shown to prevent coronary restenosis after balloon angioplasty in the MultiVitamins and Probucol (MVP) trial and other clin. studies. Probucol has also induced regression of carotid atherosclerosis in the Fukuoka Atherosclerosis Trial (FAST). However, prolongation of the QT interval with probucol remains a long-term safety concern. AGI-1067, a metabolically stable analog of probucol, is a vascular protectant (V-protectant) with strong antioxidant properties, equipotent to those of probucol. This V-protectant has been

effective in preventing atherosclerosis in all animal models tested, including low-d.-lipoprotein receptor-deficient and apolipoprotein E-knockout mice and hypercholesterolemic primates. AGI-1067 improved luminal dimensions of the percutaneous coronary intervention site (PCI) and reduced restenosis in the Canadian Antioxidant Restenosis Trial (CART-1). In contrast to probucol, AGI-1067 did not induce prolongation of the QT interval. AGI-1067 also improved luminal dimensions of the reference segments in the PCI vessels in CART-1, an effect that suggests a direct antiatherosclerosis effect. This has potentially important implications, as local approaches to prevent restenosis, such as coated stents, are not expected to prevent atherosclerosis progression, myocardial infarction, and cardiovascular death. Considering that oxidative stress and inflammation may persist for a prolonged period after stenting, treatment with AGI-1067 for the entire period of risk after PCI (instead of only 4 wk in CART-1) may result in enhanced protection against luminal renarrowing in the ongoing multicenter CART-2 trial. Because the ultimate goal of therapy for patients with coronary artery disease must remain prevention of disease progression and atherosclerosis-related events, CART-2 will test the value of AGI-1067 for the reduction of both post-PCI restenosis and atherosclerosis progression.

IT **216167-82-7**, AGI 1067
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. results with AGI-1067, a novel antioxidant cardiovascular protectant)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

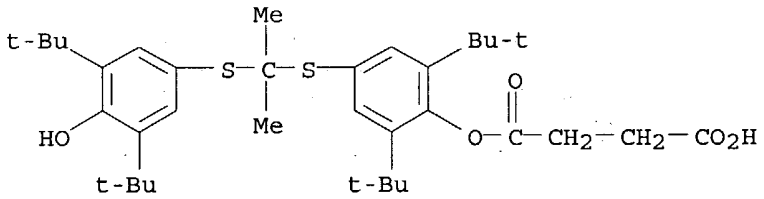
L24 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:201720 CAPLUS
DN 139:254552
TI Chemistry and pharmacology of vascular protectants: A novel approach to the treatment of atherosclerosis and coronary artery disease
AU Wasserman, Martin A.; Sundell, Cynthia L.; Kunsch, Charles; Edwards, David; Meng, Charles Q.; Medford, Russell M.
CS Department of Discovery Research, AtheroGenics, Inc., Alpharetta, GA, 30004, USA
SO American Journal of Cardiology (2003), 91(3A), 34A-40A
CODEN: AJCDAG; ISSN: 0002-9149
PB Excerpta Medica, Inc.
DT Journal; General Review
LA English
AB This review addresses the role of oxidative stress in the pathol. of atherosclerosis and why it is now believed that atherosclerosis is not only a disease of oxidative stress but also of chronic inflammation. Perhaps more importantly, this review also describes the vascular protectant (V-protectant) technol. platform originated at AtheroGenics, Inc., from which a series of inhibitory compds. has emerged to treat a number of chronic inflammatory diseases, including atherosclerosis. In

atherosclerosis, these drugs not only act as antioxidants, but also as lipid modulators, inhibitors of inflammation, and inhibitors of gene expression. It is also important to understand the basis for considering vascular cell adhesion mol.-1 (VCAM-1) as a reduction-oxidation-sensitive protein, which has a key role in the early phases of atherosclerosis. The review concludes with a description of the design and chemical of AtheroGenics' lead clin. development compound, AGI-1067, and an anal. of its preclin. in vitro and in vivo profile. AGI-1067 is a novel, potent antioxidant with anti-inflammatory properties. It inhibits gene expression of VCAM-1 and monocyte chemoattractant protein-1, decreases low-d. lipoprotein cholesterol levels, and prevents atherosclerosis in a number of animal models. AGI-1067 is currently undergoing clin. trials as an antiatherosclerotic agent.

IT **216167-82-7**, AGI-1067
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical and pharmacol. of vascular protectant AGI-1067 for treatment of atherosclerosis and coronary artery disease)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

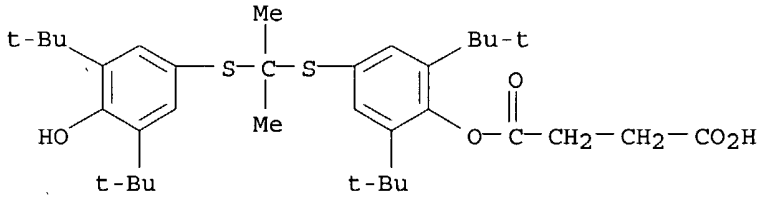
L24 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:65489 CAPLUS
DN 139:240268
TI Effects of AGI-1067 and probucol after percutaneous coronary interventions
AU Tardif, Jean-Claude; Gregoire, Jean; Schwartz, Leonard; Title, Lawrence; Laramee, Louise; Reeves, Francois; Lesperance, Jacques; Bourassa, Martial G.; L'Allier, Philippe L.; Glass, Mitchell; Lambert, Jean; Guertin, Marie-Claude
CS Montreal Heart Institute (J.C.T., J.G., J. Lesperance, M.G.B., P.L.L., J. Lambert, M.-C.G.), Montreal, Montreal, Can.
SO Circulation (2003), 107(4), 552-558
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB AGI-1067, a metabolically stable modification of probucol, is an equipotent antioxidant to probucol but is pharmacol. distinct. In a multicenter trial, we studied whether AGI-1067 reduces restenosis assessed by intravascular ultrasound (IVUS) after percutaneous coronary intervention (PCI) compared with placebo and probucol used as a pos. control. Two weeks before PCI, 305 patients were randomly assigned to 1 of 5 treatment groups: placebo, probucol 500 mg BID, or AGI-1067 70, 140, or 280 mg once daily. Patients were treated for 2 wk before and 4 wk after PCI. Baseline and 6-mo follow-up IVUS were interpreted by a blinded core laboratory Stents were used in 85% of patients. Luminal area at the PCI site at follow-up was 2.66±1.58 mm2 for placebo, 3.69±2.69 mm2 for probucol, 2.75±1.76 mm2 for AGI-1067 70 mg, 3.17±2.26 mm2 for AGI-1067 140 mg, and 3.36±2.12 mm2 for AGI-1067 280 mg (P=0.02 for the

dose-response relationship; P0.05 for AGI-1067 280 mg and probucol vs. placebo). There was a mean narrowing of 5.3 mm3 of reference segment lumen in the placebo group and an enlargement in the AGI-1067 140- and 280-mg groups at follow-up (P=0.05 for 140 mg). An increase in QTc interval >60 ms occurred in 4.8% of placebo patients, 17.4% of probucol patients, and 4.8%, 2.4%, and 2.5% of patients in the AGI-1067 groups (P=0.02). AGI-1067 and probucol reduce restenosis after PCI. In contrast to probucol, AGI-1067 did not cause prolongation of the QTc interval and improved lumen dimensions of reference segments, suggestive of a direct effect on atherosclerosis.

IT **216167-82-7**, AGI-1067
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of AGI-1067 vs. probucol after percutaneous coronary interventions)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

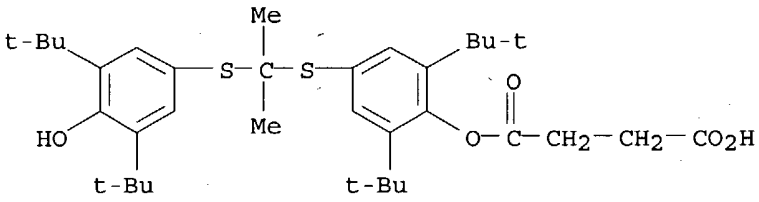
L24 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:871239 CAPLUS
DN 139:16870
TI Prevention of restenosis with antioxidants: Mechanisms and implications
AU Tardif, Jean-Claude; Gregoire, Jean; L'Allier, Philippe L.
CS Department of Medicine, Montreal Heart Institute, Montreal, Can.
SO American Journal of Cardiovascular Drugs (2002), 2(5), 323-334
CODEN: AJCDDJ; ISSN: 1175-3277
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review giving an overview of the field of restenosis prevention with antioxidants, put in the perspective of their potential use for the prevention of atherosclerosis progression. Compelling evidence points to oxidative stress as an important trigger in the complex chain of events leading to atherosclerosis. There is also evidence that oxidative stress occurs early after angioplasty. Reactive oxygen species (ROS) can induce endothelial dysfunction and macrophage activation, resulting in the release of cytokines and growth factors that stimulate matrix remodeling and smooth muscle cell proliferation. The accumulation of new extracellular matrix and smooth muscle cells will result in the neointimal formation responsible for lumen narrowing after stent deployment and which contributes to that after balloon angioplasty. In addition, oxidation processes
are involved in the crosslinking of collagen fibers, and this coupled with smooth muscle cell contraction and endothelial dysfunction may result in long-term vascular constriction or lack of adaptive vascular remodeling after balloon angioplasty. The powerful antioxidant probucol has been shown to prevent coronary restenosis after balloon angioplasty in the Multivitamins and Probucol (MVP) trial and other clin. studies. However, prolongation of the QT interval with probucol remains a long-term safety

concern. AGI-1067, a metabolically stable analog of probucol, is a vascular protectant with strong antioxidant properties as potent to those of probucol. There has been no evidence of prolongation of the QT interval with AGI-1067 in initial clin. studies. The anti-restenosis properties of AGI-1067 are being assessed in the Canadian Antioxidant Restenosis Trial (CART)-1. Considering that oxidative stress and inflammation may persist for a prolonged period after stent placement, treatment with AGI-1067 for the entire period of risk after percutaneous coronary intervention (PCI) [instead of only 4 wk in CART-1] may result in enhanced protection against luminal re-narrowing. This hypothesis will be tested in the randomized, multicenter CART-2 trial. AGI-1067 has been effective at preventing atherosclerosis in all tested animal models, including the low d. lipoprotein receptor-deficient and apo-E knockout mice. As the ultimate goal of therapy for patients with coronary artery disease must remain prevention of disease progression and atherosclerosis-related events, CART-2 will test the value of AGI-1067 for the reduction of both post-PCI restenosis and atherosclerosis progression.

IT **216167-82-7**, AGI-1067
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of prevention of restenosis with antioxidants and implications for therapy of coronary artery disease and atherosclerosis)

RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:849415 CAPLUS
DN 137:333157
TI Probucol monoesters for increasing levels and improving functionality of plasma HDL cholesterol
IN Luchoomun, Jayraz; Saxena, Uday; Sundell, Cynthia L.; Sikorski, James A.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002087556	A2	20021107	WO 2002-US12678	20020411
	WO 2002087556	A3	20030206		
	WO 2002087556	C2	20030320		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US	2003064967	A1	20030403	US 2002-122516	20020411
EP	1385501	A2	20040204	EP 2002-749523	20020411

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US 2001-283376P	P	20010411
	US 2001-345025P	P	20011109
	WO 2002-US12678	W	20020411

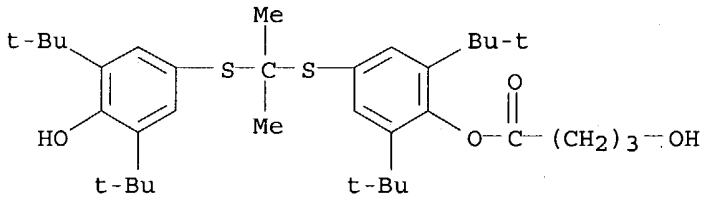
OS MARPAT 137:333157

AB It has been discovered that certain selected probucol monoesters, and their pharmaceutically acceptable salts or prodrugs, are useful for increasing circulating HDL cholesterol. These compds. may also improve HDL functionality by (a) increasing clearance of cholesteryl esters, (b) increasing HDL-particle affinity for hepatic cell surface receptors, or (c) increasing the half-life of apoAI-HDL. The pharmaceutical compns. comprise probucol monoesters alone or in combination with other agents, e.g, statins, IBAT inhibitors, MTP inhibitors, cholesterol absorption inhibitors, phytosterols, CETP inhibitors, fibric acid derivs., and antihypertensive agents. For example, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl]ester of pentanedioic acid, prepared from probucol and glutaric anhydride, elevated HDLc in hyperlipidemic hamster by 22% (average of 3 expts., range 5-44%), compared to untreated controls after 2 wk treatment at a dose of 150 mg/kg/day. LDLc was reduced by 29% on average, VLDL cholesterol by 42%, and triglycerides by 24%, compared to controls. The compound was well tolerated and all animals gained weight

IT **216167-88-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of probucol monoesters for increasing levels and improving functionality of plasma HDL cholesterol)

RN 216167-88-3 CAPLUS

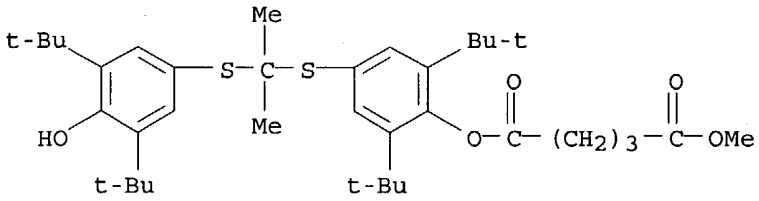
CN Butanoic acid, 4-hydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



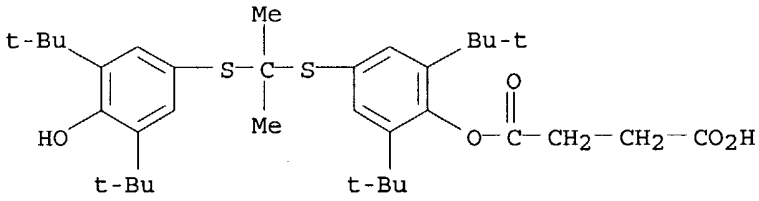
IT **216167-80-5P 216167-82-7P 216167-94-1P 474236-49-2P 474236-50-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of probucol monoesters for increasing levels and improving functionality of plasma HDL cholesterol)

RN 216167-80-5 CAPLUS

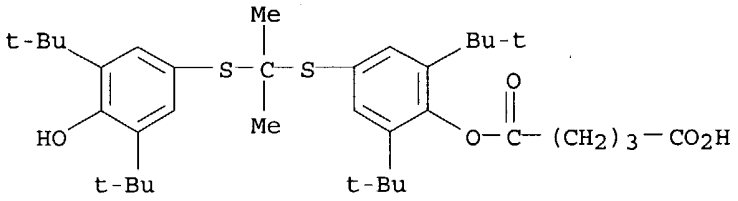
CN Pentanedioic acid, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl methyl ester (9CI) (CA INDEX NAME)



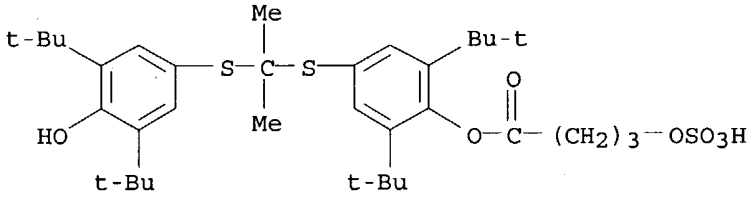
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

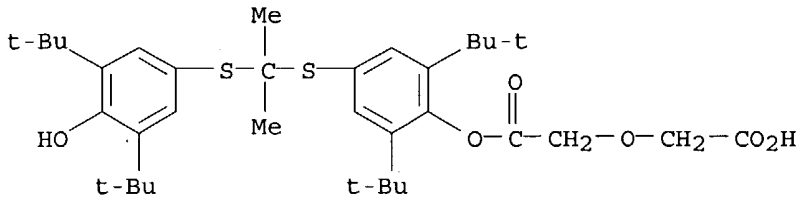


RN 474236-49-2 CAPLUS
CN Butanoic acid, 4-(sulfooxy)-, 1-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester, monosodium salt (9CI) (CA INDEX NAME)



● Na

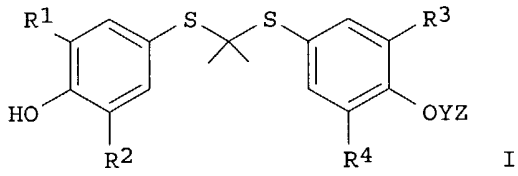
RN 474236-50-5 CAPLUS
CN Acetic acid, [2-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



L24 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814837 CAPLUS
DN 137:320305
TI Probucol derivatives and methods for treating transplant rejection
IN Edwards, David B.; Somers, Patricia K.; Glass, Mitchell
PA Atherogenics, Onc., USA
SO U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 815,262.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002156022	A1	20021024	US 2001-36307	20011025
	US 6670398	B2	20031230		
	US 6147250	A	20001114	US 1998-79213	19980514
	US 6548699	B1	20030415	US 1999-370046	19990806
	US 2002016300	A1	20020207	US 2001-815262	20010321
	US 2002177717	A1	20021128	US 2002-60734	20020130
	US 6617352	B2	20030909		
	US 2002169215	A1	20021114	US 2002-114346	20020402
	US 6602914	B2	20030805		
	US 2002188118	A1	20021212	US 2002-115206	20020402
	US 2002193446	A1	20021219	US 2002-114351	20020402
	US 2004138147	A1	20040715	US 2003-744763	20031223
PRAI	US 1997-47020P	P	19970514		
	US 1998-79213	A1	19980514		
	US 1999-370046	A2	19990806		
	US 2000-191046P	P	20000321		
	US 2001-815262	A2	20010321		
	US 2001-36307	A1	20011025		

OS MARPAT 137:320305
GI



I

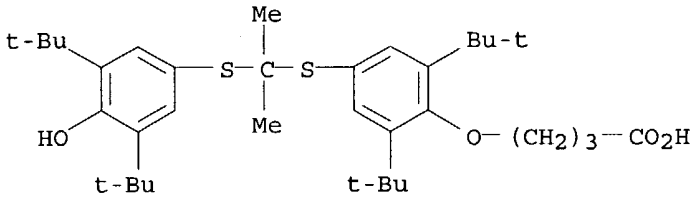
AB The invention discloses the use of I [R1-R4 = H, OH, C1-10 alkyl, aryl, heteroaryl, etc.; Y = bond, C(O); Z = C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, etc.], and pharmaceutically acceptable salts thereof, alone or in combination, for the treatment of transplant rejection. Preparation of I [R1-R4 = tert-butyl; YZ = (CH2)3COOH] from probucol which was evaluated in a graft arteriopathy model and Me 4-chlorobutyrate is described.

IT **216167-95-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(probucol derivs. for treatment of transplant rejection)

RN 216167-95-2 CAPLUS

CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



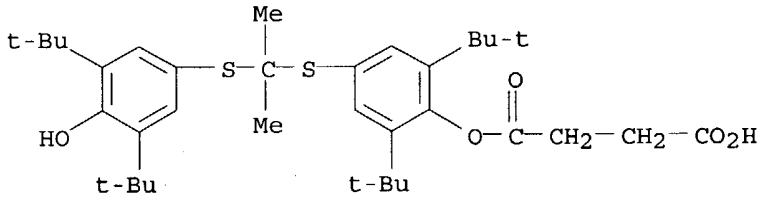
IT **216167-82-7 216167-92-9 216167-94-1**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(probucol derivs. for treatment of transplant rejection)

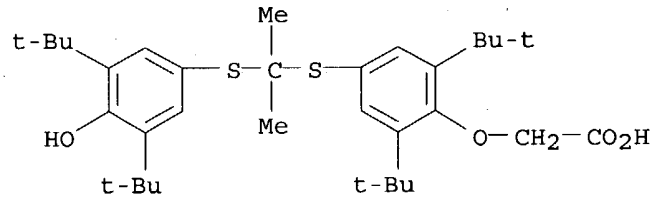
RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



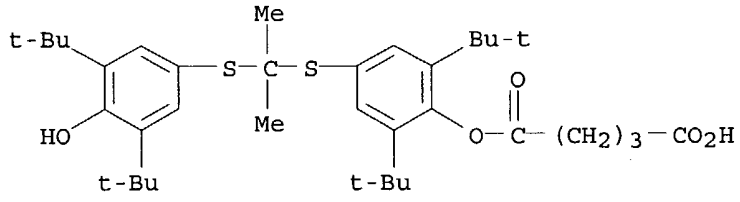
RN 216167-92-9 CAPLUS

CN Acetic acid, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)

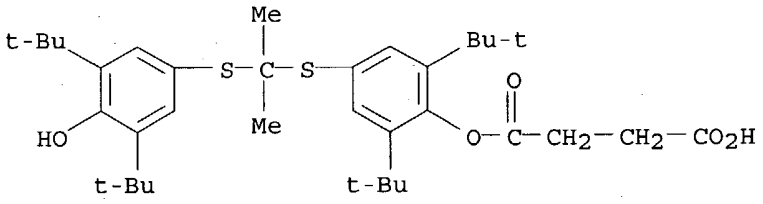


RN 216167-94-1 CAPLUS

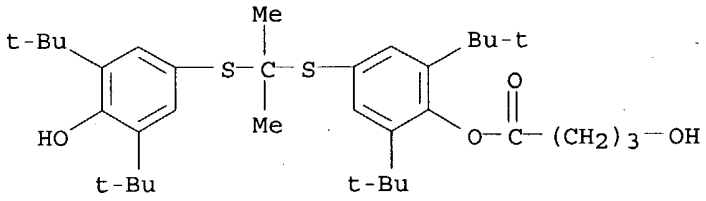
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



L24 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:641096 CAPLUS
DN 138:313884
TI Novel phenolic antioxidants as multifunctional inhibitors of inducible VCAM-1 expression for use in atherosclerosis
AU Meng, Charles Q.; Somers, Patricia K.; Rachita, Carolyn L.; Holt, Lisa A.; Hoong, Lee K.; Zheng, X. Sharon; Simpson, Jacob E.; Hill, Russell R.; Olliff, Lynda K.; Kunsch, Charles; Sundell, Cynthia L.; Parthasarathy, Sampath; Saxena, Uday; Sikorski, James A.; Wasserman, Martin A.
CS AtheroGenics, Inc., Alpharetta, GA, 30004, USA
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(18), 2545-2548
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A series of novel phenolic compds. has been discovered as potent inhibitors of TNF-α-inducible expression of vascular cell adhesion mol.-1 (VCAM-1) with concurrent antioxidant and lipid-modulating properties. Optimization of these multifunctional agents led to the identification of AGI-1067 as a clin. candidate with demonstrated efficacies in animal models of atherosclerosis and hyperlipidemia.
IT **216167-82-7**, AGI-1067 **216167-88-3 216167-94-1**
216168-38-6 216168-43-3 219773-27-0
474236-50-5 512790-96-4 512790-97-5
512790-98-6 512790-99-7 512791-00-3
512791-01-4 512791-03-6 512791-04-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic antioxidants as inhibitors of inducible VCAM-1 expression for use in atherosclerosis)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

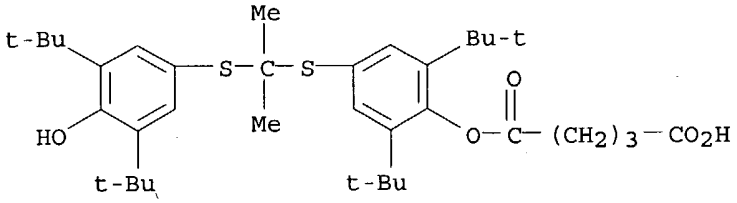


RN 216167-88-3 CAPLUS
CN Butanoic acid, 4-hydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)

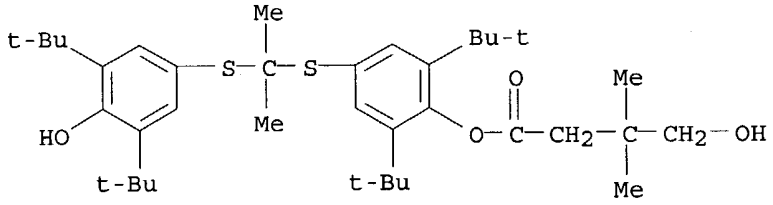


RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl]

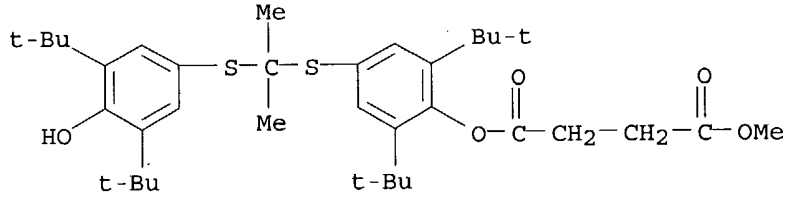
ester (9CI) (CA INDEX NAME)



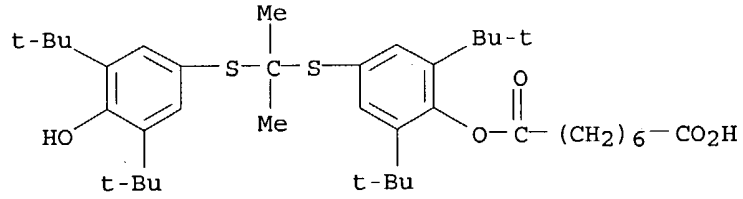
RN 216168-38-6 CAPLUS
CN Butanoic acid, 4-hydroxy-3,3-dimethyl-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



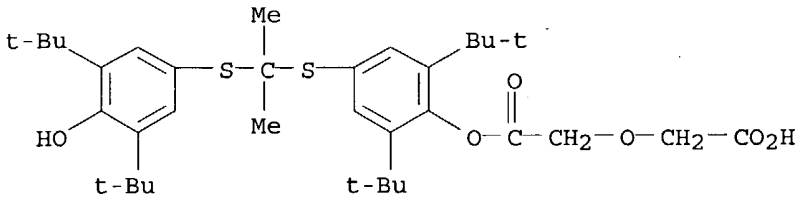
RN 216168-43-3 CAPLUS
CN Butanedioic acid, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl methyl ester (9CI) (CA INDEX NAME)



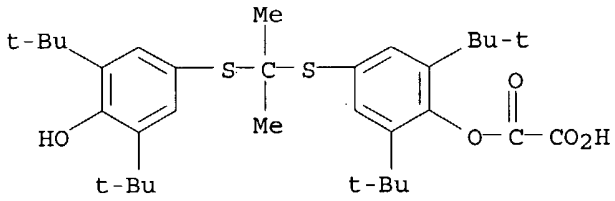
RN 219773-27-0 CAPLUS
CN Octanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 474236-50-5 CAPLUS
CN Acetic acid, [2-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

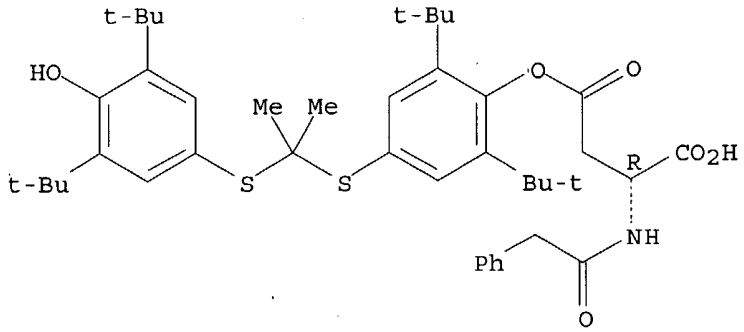


RN 512790-96-4 CAPLUS
CN Ethanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

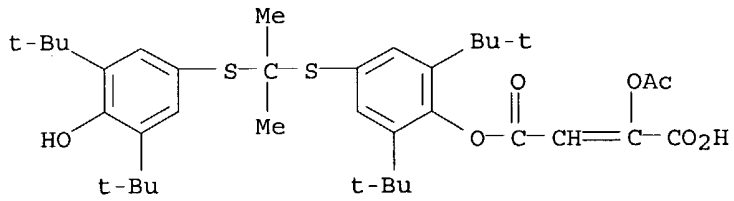


RN 512790-97-5 CAPLUS
CN D-Aspartic acid, N-(phenylacetyl)-, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

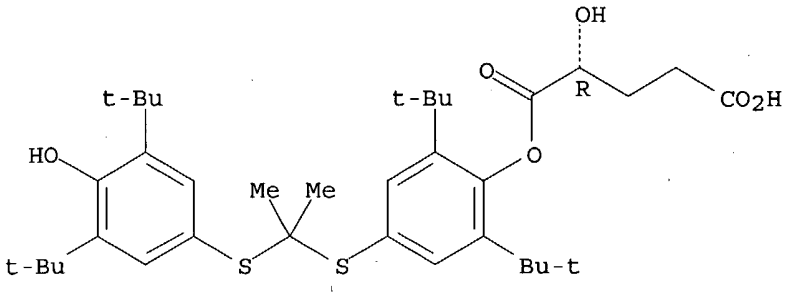


RN 512790-98-6 CAPLUS
CN 2-Butenedioic acid, 2-(acetyloxy)-, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

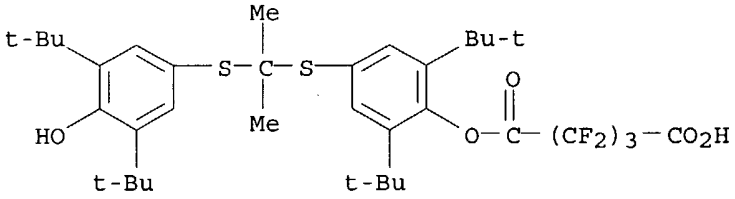


RN 512790-99-7 CAPLUS
CN Pentanedioic acid, 2-hydroxy-, 1-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester, (2R)- (9CI) (CA INDEX NAME)

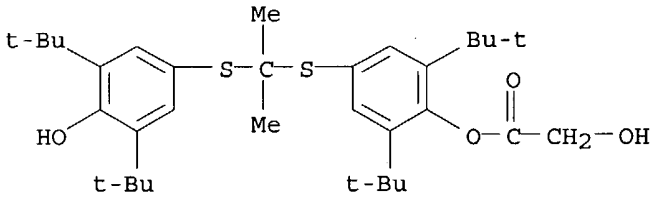
Absolute stereochemistry.



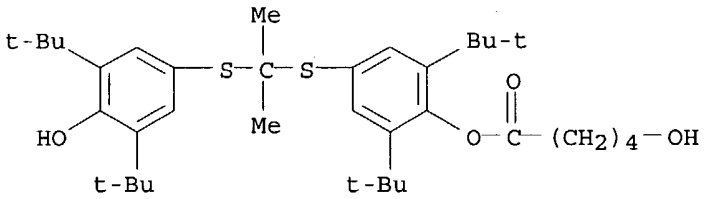
RN 512791-00-3 CAPLUS
CN Pentanedioic acid, hexafluoro-, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



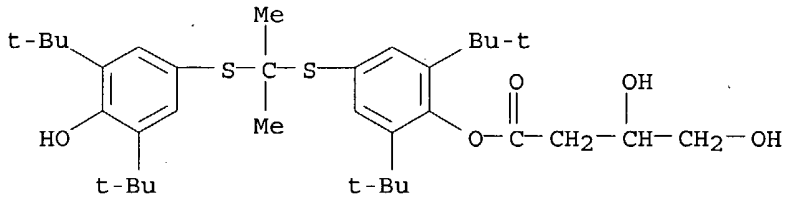
RN 512791-01-4 CAPLUS
CN Acetic acid, hydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



RN 512791-03-6 CAPLUS
CN Pentanoic acid, 5-hydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)

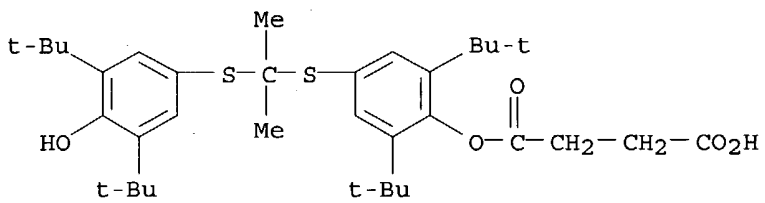


RN 512791-04-7 CAPLUS
CN Butanoic acid, 3,4-dihydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:580040 CAPLUS
DN 138:130391
TI AGI-1067 AtheroGenics
AU Hatch, Grant M.
CS Department of Pharmacology and Therapeutics Faculty of Medicine, University of Manitoba, Winnipeg, MB, R3E 0T6, Can.
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(3), 433-436
CODEN: COIDAZ; ISSN: 1472-4472
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review. AGI-1067 is an oral VCAM-1 (vascular cell adhesion mol.-1) gene expression inhibitor under development by AtheroGenics for the potential prevention of atherosclerosis (hypercholesterolemia) and restenosis. AGI-1067 was also being developed in collaboration with Schering-Plough; however, in Oct. 2001, all rights to the drug were returned to AtheroGenics. In Feb. 2001, dosing was completed in phase II trials for the potential treatment and prevention of restenosis and atherosclerosis following angioplasty. In Dec. 2001, further phase II trials (CART-2) were initiated for the treatment of restenosis and atherosclerosis. Early-phase clin. trials are ongoing for the prevention of atherosclerosis. In Jan. 2002, analysts at Adams, Harkness & Hill predicted that AGI-1067 would be launched in the second half of 2005, with sales of US $100 m in that year and US $540 m in 2006. It was also believed that AtheroGenics would look to sign a marketing partnership following the expected completion of the CART-2 trial in 2002.
IT **216167-82-7**, AGI 1067
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AGI-1067 pharmacol. and clin. development)
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

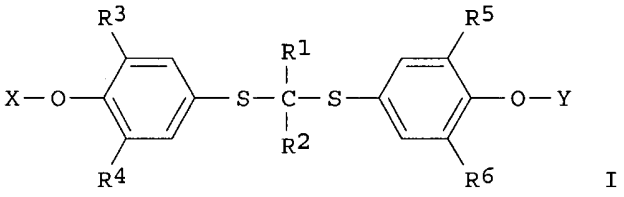


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

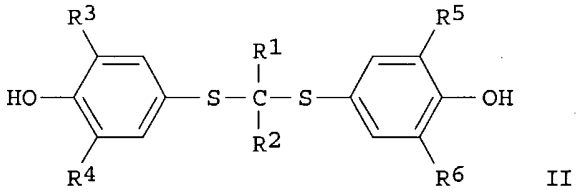
L24 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:863541 CAPLUS
DN 135:371524
TI Process for preparing water-soluble probucol acyl esters for use as food antioxidants
IN Jass, Paul Alan
PA Salsbury Chemicals, Inc., USA
SO U.S., 5 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6323359	B1	20011127	US 2000-562657	20000502

PRAI US 2000-562657 20000502
OS CASREACT 135:371524; MARPAT 135:371524
GI



I

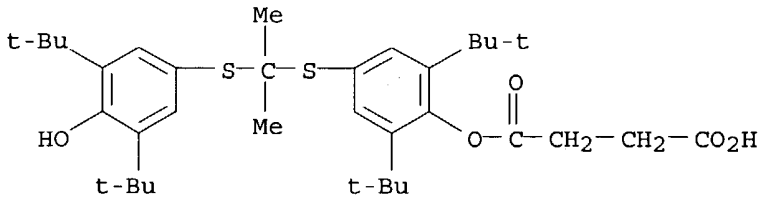


II

AB Water-soluble derivs. of probucol compds. [I; R1, R2 = alkyl, alkenyl, aryl; R3-R6 = C1-4 alkyl; X, Y = H, (un)saturated (un)substituted C1-8 acyl] (e.g., probucol mono- and disuccinate), useful as food antioxidants, are prepared by the reaction of a solution of a probucol compound (II) with an alkali metal hydroxide, alkali metal alkoxide (e.g., potassium tert-butoxide), alkylammonium alkoxide, alkylammonium hydroxide and mixts. forming an ammonium or an alkali metal salt of the probucol compound and reacting the salt with a carboxylic acid anhydride selected from succinic anhydride, glutaric anhydride, adipic anhydride, suberic anhydride, sebacic anhydride, azelaic anhydride, phthalic anhydride, and maleic anhydride.

IT **216167-82-7P**
RL: FFD (Food or feed use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing water-soluble probucol acyl esters for use as food antioxidants)

RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

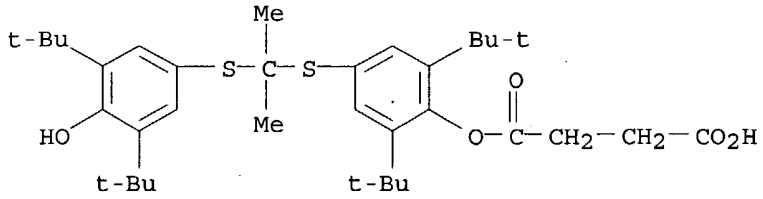
L24 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:335659 CAPLUS
DN 132:343330
TI Methods and compositions to lower plasma cholesterol levels
IN Medford, Russell M.; Saxena, Uday
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000028332	A1	20000518	WO 1999-US26519	19991109
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1137948	A1	20011004	EP 1999-962732	19991109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002529740	T2	20020910	JP 2000-581459	19991109
PRAI	US 1998-107644P	P	19981109		
	WO 1999-US26519	W	19991109		

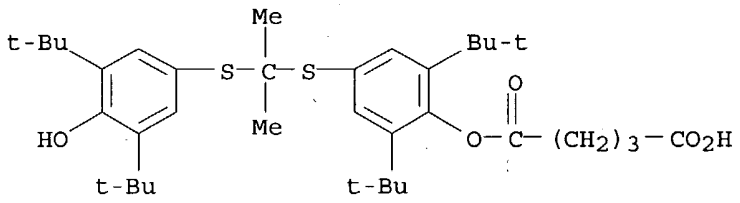
AB A method for determining whether a compound binds to a lipoprotein, e.g. LDL or VLDL, in a manner which will lower plasma cholesterol is provided that includes assessing the ability of the compound to form a complex with the lipoprotein, e.g., LDL or VLDL, and then determining whether the newly formed complex causes a change in the structure of apoB-100 that results in increased binding affinity to the LDL receptor. Also disclosed is a method for lowering cholesterol in a host in need thereof, including a human, that includes the administration of an effective amount of a compound which binds to cholesterol-carrying lipoprotein (e.g. LDL or VLDL) in a manner that alters the three dimensional configuration of the lipoprotein and increases the binding affinity of the apoB-100 protein to the LDL receptor, including those on the surface of a hepatic cell.

IT **216167-82-7 216167-94-1 216167-95-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. to lower plasma cholesterol levels)

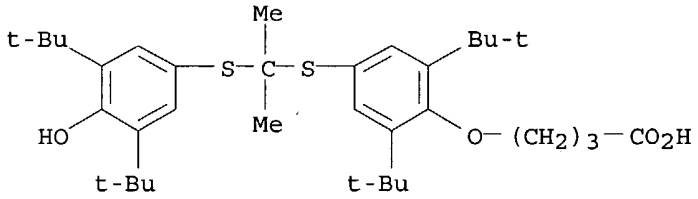
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 216167-95-2 CAPLUS
CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:48609 CAPLUS
DN 130:119591
TI Antioxidant enhancement of therapy for hyperproliferative conditions
IN Chinery, Rebecca; Beauchamp, R. Daniel; Coffey, Robert J.; Medford, Russell M.; Wadsinski, Brian
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9901118	A2	19990114	WO 1998-US13750	19980701
	WO 9901118	A3	19990422		

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

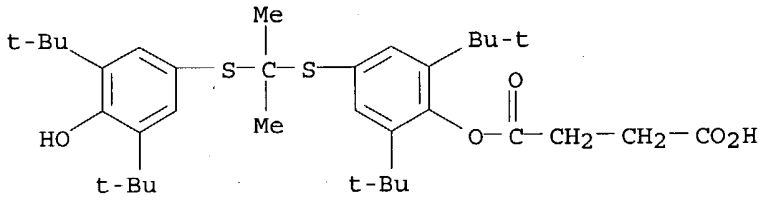
	AU 9882827	A1	19990125	AU 1998-82827	19980701
	EP 1019034	A2	20000719	EP 1998-933078	19980701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002511878	T2	20020416	JP 1999-507360	19980701
	US 2001049349	A1	20011206	US 2001-779086	20010207
PRAI	US 1997-886653	A	19970701		
	US 1997-967492	A	19971111		
	US 1998-108609	B1	19980701		
	WO 1998-US13750	W	19980701		

OS MARPAT 130:119591

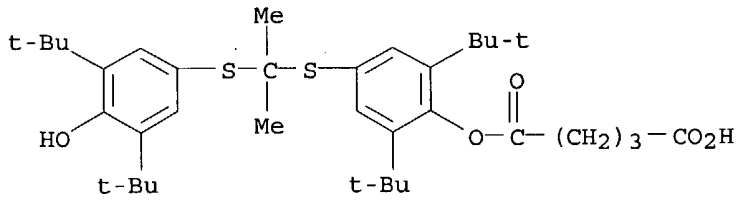
AB A method to enhance the cytotoxic activity of an antineoplastic drug comprises administering an effective amount of the antineoplastic drug to a host exhibiting abnormal cell proliferation in combination with an effective cytotoxicity-increasing amount of an antioxidant. The invention also includes a method to decrease the toxicity to an antineoplastic agent or increase the therapeutic index of an antineoplastic agent administered for the treatment of a solid growth of abnormally proliferating cells, comprising administering an antioxidant prior to, with, or following the antineoplastic treatment.

IT **216167-82-7 216167-94-1 219773-26-9 219773-27-0 219773-28-1 219773-29-2 219773-30-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant enhancement of therapy for hyperproliferative conditions)

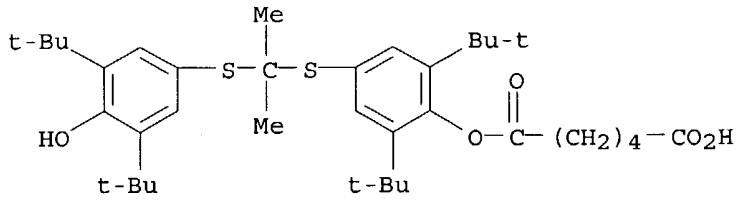
RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



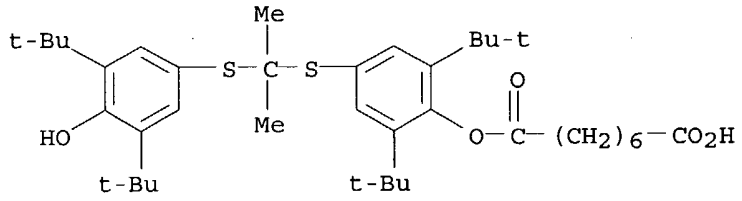
RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



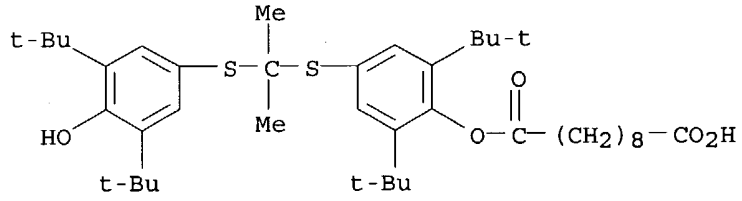
RN 219773-26-9 CAPLUS
CN Hexanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



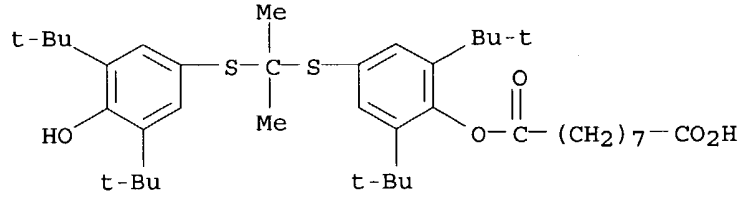
RN 219773-27-0 CAPLUS
CN Octanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 219773-28-1 CAPLUS
CN Decanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

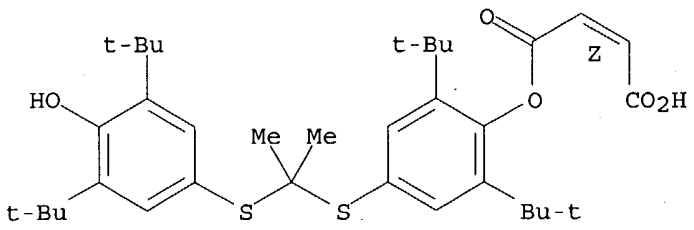


RN 219773-29-2 CAPLUS
CN Nonanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



RN 219773-30-5 CAPLUS
CN 2-Butenedioic acid (2Z)-, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

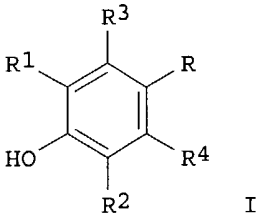
Double bond geometry as shown.



L24 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:761875 CAPLUS
DN 130:13646
TI Preparation of phenolic compounds for the inhibition of the expression of VCAM-1
IN Medford, Russell M.; Somers, Patricia K.; Hoong, Lee K.; Meng, Charles Q.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9851662	A2	19981119	WO 1998-US9781	19980514
	WO 9851662	A3	20000302		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2428130	AA	19981119	CA 1998-2428130	19980514
	AU 9874851	A1	19981208	AU 1998-74851	19980514
	AU 750041	B2	20020711		
	TR 9902802	T2	20000421	TR 1999-9902802	19980514
	EP 994853	A2	20000426	EP 1998-922264	19980514
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 9902803	T2	20000721	TR 1999-9902803	19980514
	US 6121319	A	20000919	US 1998-78935	19980514
	BR 9809819	A	20010918	BR 1998-9819	19980514
	JP 2002503227	T2	20020129	JP 1998-549502	19980514
	NO 9905544	A	20000110	NO 1999-5544	19991112
	MX 9910402	A	20000630	MX 1999-10402	19991112
	NO 2003002254	A	20000110	NO 2003-2254	20030519
PRAI	US 1997-47020P	P	19970514		
	WO 1998-US9781	W	19980514		

OS MARPAT 130:13646
GI



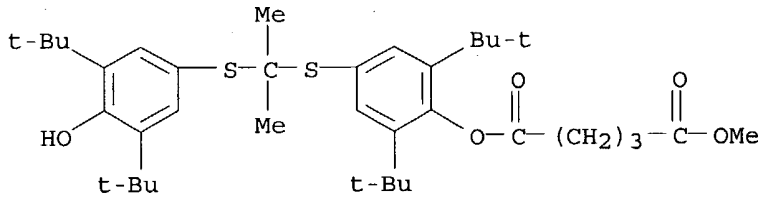
I

AB Title compds. [e.g., I; R = Z1Z2R5; R1,R2 = (un)substituted (cyclo)alkyl, -(hetero)aryl, etc.; R3,R4 = any group that does not otherwise adversely affect (sic) the desired properties of the mol. including H, halogen, or R1 (sic); R5 = (di)(alkyl)amino, alkyl, alkoxy(carbonyl), (hetero)aryl, etc.; Z1 = O SO0-2, NH, CH2; Z2 = bond, alkylene(oxy) aryleneoxy, etc.] were prepared Thus, 4-(BrCH2)C6H4CH2CO2H was thioetherified by 4-mercapto-2,6-di-tert-butylphenol to give I [R = SCH2C6H4(CH2CO2H)-4, R1 = R2 = CMe3, R3 = R4 = H]. Data for biol. activity of I were given.

IT **216167-80-5P 216167-82-7P 216167-88-3P 216167-92-9P 216167-94-1P 216167-95-2P 216168-18-2P 216168-37-5P 216168-38-6P 216168-39-7P 216168-41-1P 216168-43-3P 216168-44-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenolic compds. for the inhibition of the expression of VCAM-1)

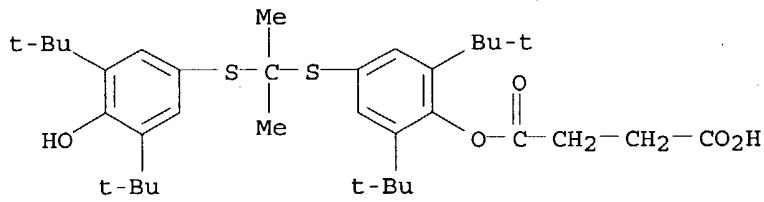
RN 216167-80-5 CAPLUS

CN Pentanedioic acid, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl methyl ester (9CI) (CA INDEX NAME)



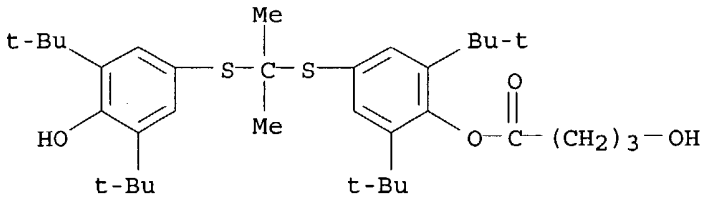
RN 216167-82-7 CAPLUS

CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)

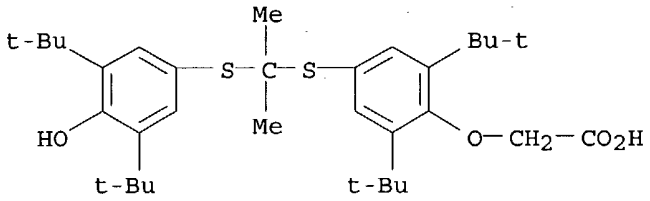


RN 216167-88-3 CAPLUS

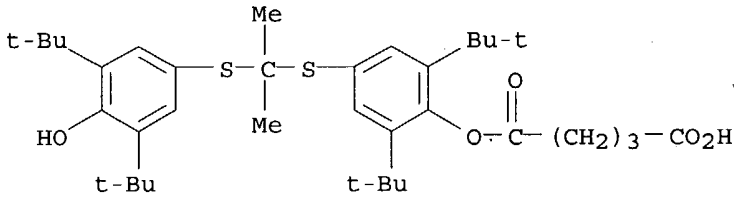
CN Butanoic acid, 4-hydroxy-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



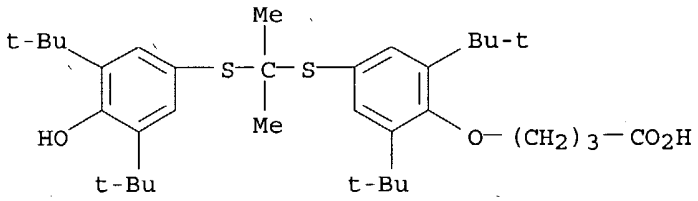
RN 216167-92-9 CAPLUS
CN Acetic acid, [4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 216167-94-1 CAPLUS
CN Pentanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



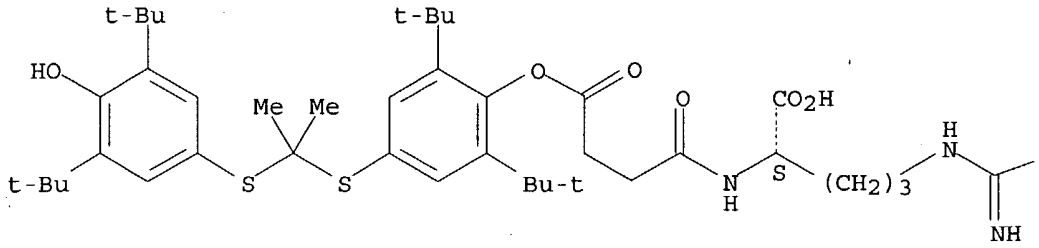
RN 216167-95-2 CAPLUS
CN Butanoic acid, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 216168-18-2 CAPLUS
CN L-Arginine, N2-[4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]-1,4-dioxobutyl]- (9CI) (CA INDEX NAME)

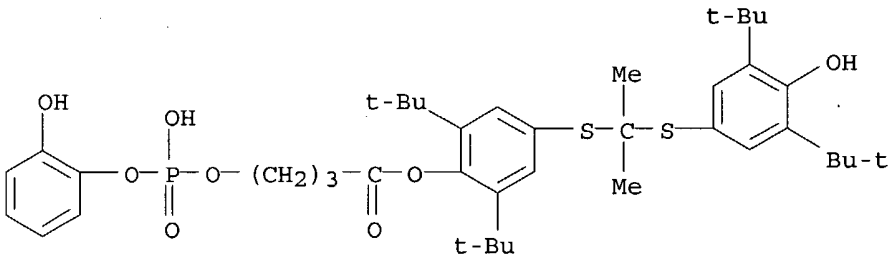
Absolute stereochemistry.

PAGE 1-A

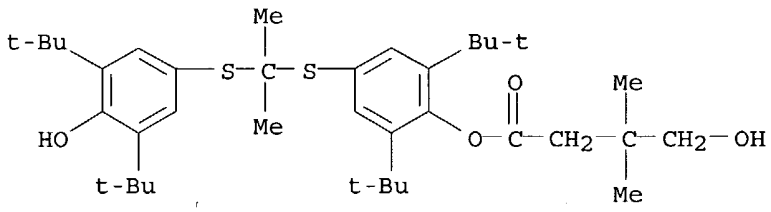


PAGE 1-B

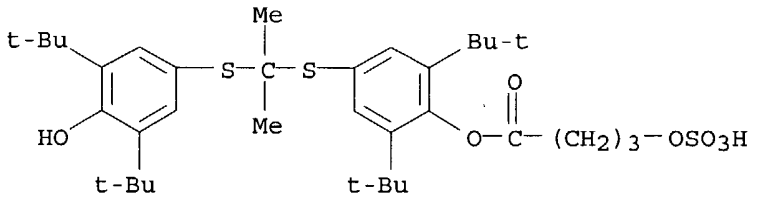
RN 216168-37-5 CAPLUS
CN Butanoic acid, 4-[[hydroxy(2-hydroxyphenoxy)phosphinyl]oxy]-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



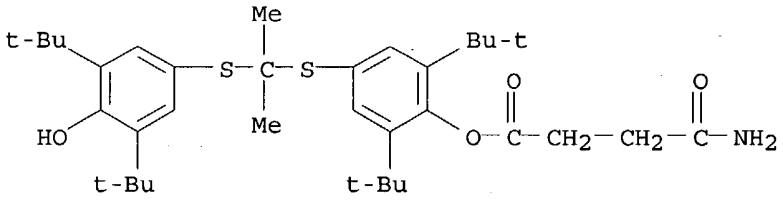
RN 216168-38-6 CAPLUS
CN Butanoic acid, 4-hydroxy-3,3-dimethyl-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



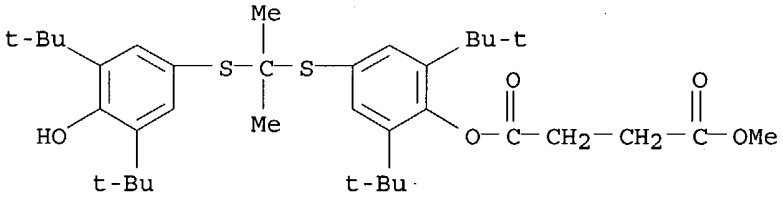
RN 216168-39-7 CAPLUS
CN Butanoic acid, 4-(sulfooxy)-, 1-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



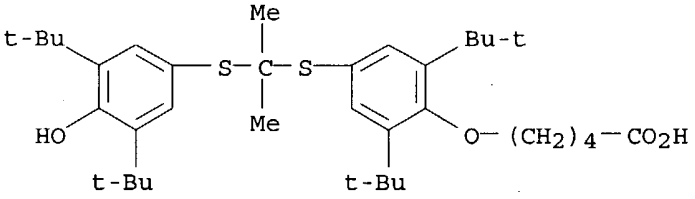
RN 216168-41-1 CAPLUS
CN Butanoic acid, 4-amino-4-oxo-, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl ester (9CI) (CA INDEX NAME)



RN 216168-43-3 CAPLUS
CN Butanedioic acid, 4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl methyl ester (9CI) (CA INDEX NAME)

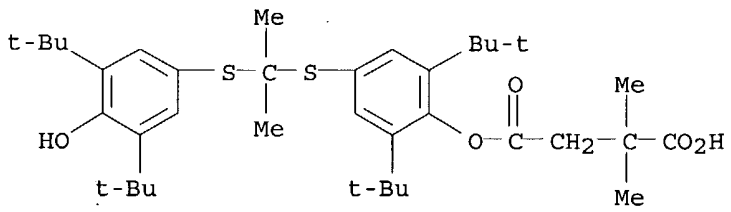


RN 216168-44-4 CAPLUS
CN Pentanoic acid, 5-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenoxy]- (9CI) (CA INDEX NAME)



IT **216168-63-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenolic compds. for the inhibition of the expression of VCAM-1)

RN 216168-63-7 CAPLUS
CN Butanedioic acid, 2,2-dimethyl-, 4-[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl] ester (9CI) (CA INDEX NAME)



L24 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:761806 CAPLUS
DN 130:20572
TI Monoesters of probucol for the treatment of cardiovascular and inflammatory disease
IN Medford, Russell M.; Somers, Patricia K.
PA Atherogenics, Inc., USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9851289	A2	19981119	WO 1998-US9773	19980514
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	US 6121319	A	20000919	US 1998-78935	19980514
	JP 2001524986	T2	20011204	JP 1998-549498	19980514
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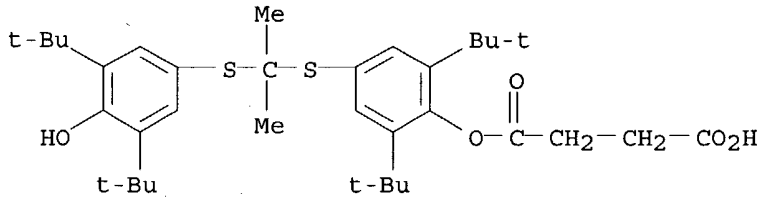
AB This invention is a method and composition for the inhibition of VCAM-1, and in particular for the treatment of cardiovascular or inflammatory disease, including atherosclerosis, that includes the administration of an effective amount of an ester of probucol. Rabbits were fed high fat chow (0.5% cholesterol and 3% coconut oil) containing 0.5% probucol monosuccinate (I) for 3wk. I caused a significant reduction in all lipoprotein fractions.

IT **216167-82-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoesters of probucol for treatment of cardiovascular and inflammatory disease)

RN 216167-82-7 CAPLUS
CN Butanedioic acid, mono[4-[[1-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-1-methylethyl]thio]-2,6-bis(1,1-dimethylethyl)phenyl]

ester (9CI) (CA INDEX NAME)



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